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BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

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SUMMARY OF RECENT ABSTRACTS*

VII. HELMINTHIASIS

Trematodes

Schistosomiasis, general.—COWPER (p. 217) has written on the maintenance and breeding in Britain of snail hosts of schistosomes; for details the original should be consulted.

MUKERJI *et al.* (p. 599) have been unable to transmit *S. haematobium* and *S. mansoni*, from African troops, through the common Indian snails.

KHALIL and HILMY (p. 97) describe a palm-leaf snail trap which is used in Egypt to measure the intensity of snail infestation in water-courses before and after eradication has been attempted. For details the original abstract should be consulted.

BARLOW and ABDEL AZIM (p. 831), reporting on the control programme in Egypt, make the point that winter closure of irrigation canals causes a high proportion of infected snails to die. Copper sulphate is used, and the authors (p. 832) state that there is no advantage in using lime and other chemicals which they have tested. The use of palm-leaf traps in streams lacking vegetation is advantageous. They report considerable reductions in stream infestation as a result of the various measures taken. In experimental work, no infection was achieved with cercariae 48 hours old (compare ALVES below).

Gammexane is lethal to *Bulinus* and *Planorbis* in Egypt in concentrations of 5–6 p.p.m. acting for 24 hours. HALAWANI (p. 331) thinks that much smaller doses would suffice if applied for a longer time. The same author (p. 667) claims that the *delta* isomer of benzene hexachloride is effective against *Bulinus* and *Planorbis* in a dilution of 5 parts per million.

Schistosoma haematobium.—STEPHENSON (p. 598) describes the schistosomiasis position in the Gezira area of the Sudan, where the land is irrigated from the great dam at Sennar. There are 2,600 miles of irrigation channels, some of which are used only by day, others throughout the 24 hours. There has apparently been a great increase in the infestation rate with *S. haematobium*, and 21 per cent. of adults and 45 per cent. of children are infested. *S. mansoni* is present in 5 per cent. in some places, but no one method of stool examination will reveal all cases. The position seems to be deteriorating, and treatment

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v. 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

campaigns, construction of latrines, siting of villages away from canals, and propaganda have not succeeded in controlling the disease. Snail-clearance, as practised in Egypt, is needed.

BUCKLEY (p. 909) has made a survey of N. Rhodesia in which he found *S. haematobium* infection in up to 60 per cent. of the people, children showing higher figures than adults. *Physopsis globosa* and *P. africana* are the snail hosts; they are essentially inhabitants of small streams, and are scarce in large rivers, lakes or swamps.

MAKAR (p. 1010) writes on the pathology and treatment of carcinoma of the bladder in Egypt, which is probably associa ed aetiologically with *S. haematobium* infection. Other papers on schistosomiasis and cancer have been written by SCANDER Bey (p. 1010), ONSY Bey (p. 1011) and MAKAR and FAWZY (p. 1011).

ALVES and BLAIR (p. 826) describe the preparation of an antigen from cercariae of *S. haematobium*. This is used for the intradermal test and is valid for *S. haematobium* or *S. mansoni* infections. In a large series of persons tested, there were no negative results in those excreting eggs, and eggs were found in a large proportion (increasing as examinations were repeated) of those with positive tests to this antigen. The authors therefore consider the test to be accurate enough for diagnostic use in mass treatment campaigns in S. Rhodesia, where the intensive treatment with sodium antimonyl tartrate is practised. Negative reactors are probably free from the disease.

A description of the field work done during 1946 in S. Rhodesia is given by ALVES and BLAIR (p. 827), who, by the intradermal test referred to above, have found infection in 24–41 per cent. of Europeans and 13–89 per cent. of Africans. They treated 5,455 infected persons by intensive courses of sodium antimonyl tartrate (total dose 1 grain to 20 lb. body weight, divided into 3 parts and injected, in very dilute solution and very slowly, at intervals of 3 hours). There were no deaths from the drug, but the technique of administration is of the greatest importance. For snail control they used copper sulphate, of which a concentration of 5 p.p.m. kills all snails in 24 hours in the laboratory; it is much more effective than malachite. The control work should be done in the dry season in S. Rhodesia.

ALVES (p. 829) reports that GORMAN has discovered that schistosome cercariae may live as long as 144 hours in cold weather, and be infective for 96. The old idea that by storing water for 48 hours, free from snails, it is rendered harmless for schistosomiasis, cannot now be accepted.

SEITZ (p. 829) has treated 322 patients, mostly with *S. haematobium* infection, by an intensive method similar to that used by Alves and Blair, without serious reaction, and with good results.

BARTTER *et al.* (p. 1012) show that blood levels of tartar emetic fall very rapidly, and that excretion by urine (80 per cent.) and faeces (20 per cent.) is rapid. Experience with multiple injections suggests that it is possible to maintain a higher blood level by controlling the size and frequency of doses.

HALAWANI and ABDALLAH (p. 220) gave Repodral (an American preparation identical with Fouadin) 3 times a day for 2 days, to Egyptian patients with *S. haematobium* infections, with some success. The total dose was 0·5 cc. (of 6·3 per cent. solution) per kgm., divided into 6 parts. This intensive treatment is probably safer than the intensive treatment with tartar emetic, in view of the prevalence of bilharzial cirrhosis and nutritional deficiencies in Egypt. [The Repodral was presumably given by intramuscular injection, but this is not made clear by the authors.] HAMMOUDA (p. 221) examined the hearts of these patients, by electrocardiography, but any changes found were slight and transient. HALAWANI and HAFIZ (p. 329) prepare a 6·5 per cent. solution of Repodral solution immediately before use. This solution should be used on the day of preparation. Toxic symptoms are generally mild. EL AYADI

(p. 433) shows that after an intensive two-day course of Reprodral (Fouadin, Stibophen), much of the antimony was concentrated in the liver. A cumulative effect was clearly demonstrated. GELLHORN *et al.* (p. 334) discuss the tissue distribution and excretion of certain organic antimonials in hamsters; for details the original should be consulted.

RITCHKEN and KANTOR (p. 1078) report a few cases of herpes zoster in patients treated by the intensive course of intravenous antimony injections; they discuss its aetiology.

WOOD (p. 914) reports on the pharmacology of Miracil, the new drug which is claimed to be active against schistosomes.

S. mansoni.—In N. Rhodesia BUCKLEY (p. 909) found *S. mansoni* in up to 61 per cent. of people. In general the areas of high incidence with *S. mansoni* were not those with high incidence of *S. haematobium*, and children were not specially affected. It was common to find eggs in faeces without blood or mucus, and the disease appears to be very insidious. The snail host is probably *Biomphalaria pfeifferi*; evidence regarding the closely allied *B. tetragonostoma* is inconclusive. These snails are found in small streams, but are scarce in lakes and swamps.

SCHWETZ (p. 1009) found that about 10 per cent. of 317 persons examined along the Bushimaie river in the Belgian Congo had intestinal schistosomiasis, and found *Planorbis adowensis* and *Bulinus forskali* in the neighbourhood.

SCHWETZ and DARTEVELLE (p. 825 *bis*) discuss the snail hosts of *S. mansoni* in the eastern part of the Belgian Congo, and give some information on their ecology. [In the original abstracts *Planorbis boissyi tanganikanus* was misspelt *tanganikus*.]

RODRIGUEZ-MOLINA and SCHWACHMAN (p. 829) found *S. mansoni* in 14·6 per cent. of a large number of recruits in Porto Rico. They treated a number with Fouadin, but the end results after 24 months were not good—more than half the men still excreted eggs, though some of them had had as many as 6 courses of the drug. PONCE PINEDO (p. 826) reports the first known autochthonous cases of *S. mansoni* infection in the Republic of Santo Domingo.

LUTTERMOSER (p. 1078) has contributed a comprehensive account of schistosomiasis in Venezuela, where the disease is well established in certain States. The snail host is *Australorbis glabratus*, and in the programme of control, treatment, drainage of land, application of lime and other chemicals to kill snails and the development of good methods of disposal of faeces are prominent features.

JAFFÉ and FERRO (p. 433) discuss the diagnosis of schistosomiasis in post mortem material in Venezuela, comparing different techniques for the demonstration of ova in liver and rectum. By various means they obtained positive results in 34 of 86 cadavers.

S. mansoni infection is very widespread in Brazil; PINTO and DE ALMEIDA (p. 96) give a list of 198 foci already found, chiefly in the State of Pernambuco. CANÇADO (p. 912) reports on the distribution of *S. mansoni* in the State of Minas Geraes, Brazil.

PINTO (p. 216) relates a focus of *S. mansoni* infection near Rio de Janeiro to watercress gardens contaminated with human faeces, and harbouring *Australorbis glabratus*. PINTO and DE ALMEIDA (p. 216) give a list of other occupations which carry special risk—washerwomen, workmen building bridges, engineers, topographers, fishermen, and persons, young and old, who break down the *guaxima* tree for fibre, standing in water to do so. The snail hosts in Brazil are *A. glabratus* and *A. olivaceus*.

CRAM and FILES (p. 217) have confirmed previous findings that a species of *Tropicorbis* found in Louisiana is capable of acting as host for *S. mansoni*; various other species tested could not be incriminated. In an investigation of

a number of species of snails found in the Eastern United States, which STUNKARD (p. 432) attempted to infect with the three human schistosomes, no evidence was found that any could act as an intermediate host for any of the trematodes.

Snails normally liberate cercariae once each day, around midday, but KUNTZ (p. 330) has been able to force *A. glabratus* to shed cercariae of *S. mansoni* more often, by exposing them to various intensities and periods of light, and to different temperatures. Abrupt changes in temperature exert more influence than abrupt changes in light intensity.

HASHEM (p. 730) discusses Egyptian hepato-splenomegaly, which is endemic in an area roughly corresponding to that of *S. mansoni* infection. In all cases at post mortem, in which eggs could be differentiated in the liver, they were eggs of *S. mansoni*, and this trematode is the cause of the condition four times as often as *S. haematobium*. In schistosomal cirrhosis the fibrosis is essentially interstitial, and is due to infiltration in and around the fine portal tracts by eggs or even adult worms. ERFAN (p. 913) describes the pathology of the liver in schistosomiasis; in Egypt, eggs of *S. mansoni* are found more than 4 times as often as eggs of *S. haematobium* in hepatic schistosomiasis. He also describes the symptoms of these infections, and the course they take. For details the original should be consulted.

HALAWANI *et al.* (p. 99) show that in long-standing intestinal schistosomiasis with liver changes and enlarged spleen, the cephalin flocculation test and the colloidal gold test are often positive.

IGNACIO BALDO *et al.* (p. 1077) have examined by X-ray the lungs of a number of children infected with *S. mansoni*. Changes were found in about half, but seem to have been somewhat indefinite. There was evidence of myocarditis, with enlargement of the heart, in some.

WELLER and DAMMIN (p. 98) use a wetting agent (Triton NE) with the acid-ether centrifugation technique, for the examination of faeces for eggs of *S. mansoni*. By this means they found eggs in 105 of 500 specimens; without the wetting agent only 84 gave positive results. OLIVER-GONZÁLEZ and HERNÁNDEZ MORALES (p. 830) describe their method of examination of faeces for eggs of *S. mansoni* by a sedimentation technique which enables them to distinguish microscopically between living and dead eggs by observing the movements of the flame cells. They have applied this to patients after treatment with anthiomaline or urea stibamine; the simultaneous disappearance of living and dead eggs suggests that dead eggs are either laid dead or die in transit from the place where they are laid. Dead eggs found in faeces are not necessarily eggs which have been a long time in the mucosa.

HERNÁNDEZ MORALES *et al.* (p. 330) find rectal biopsy much more accurate for the diagnosis of *S. mansoni* infections than either concentration methods of stool examinations, or antigenic skin tests. WELLER (p. 599) has designed a rectal scraper, which, although not so effective for the diagnosis of *S. mansoni* infection as the acid-ether concentration method, may be a useful complement.

CULBERTSON *et al.* (p. 912) show that extracts of cercariae of *S. mansoni* and of two other worms (not parasitic in man) possess a common antigen which can be used for skin tests in schistosomiasis and other trematode infections. PRATT and OLIVER GONZÁLEZ (p. 826) show that antigens prepared from cercariae of *S. mansoni* do not lose potency for intradermal tests if stored at 6°C. for 12 months. GOLDSTEIN (p. 328) describes an antigen he prepared by extracting adult *S. bovis* in saline. He has used this as an intradermal test for intestinal schistosomiasis. It is apparently useful, but the series tested was very small.

LÔBO (p. 914) regards palpable thickening of the sigmoid colon as a useful diagnostic sign of *S. mansoni* infection.

HERNÁNDEZ MORALES *et al.* (p. 731) find tartar emetic more effective than Fouadin in the treatment of *S. mansoni* infections, provided that 1 per cent. solution is given intravenously in doses of 5 cc. to a total of at least 120 cc., the injections being given on alternate days. A second course may be necessary.

HERNÁNDEZ MORALES *et al.* (p. 218) have used Anthiomaline in the treatment of *S. mansoni* infections in Porto Rico. Given by intramuscular injection in doses of 3 cc. (*i.e.* 10 mgm. antimony) on alternate days, to a total dosage of 45–48 cc., it rarely produces serious toxic reactions, and appears to be quite effective against the infection.

For the refractory proctitis often left after treatment of intestinal schistosomiasis, RADNA (p. 99) has used histidine injections with success.

BRANDT (p. 667) has found that adult *S. mansoni* can be removed from the portal vein of heparinized rabbits more easily than from non-heparinized rabbits, and suggests that heparin can be given to mobilize the worms, followed by introduction of an anthelmintic into the portal vein at operation.

KUNTZ and STIREWALT (p. 434) have tested DDT against cercariae of *S. mansoni*. Its cercaricidal power is so slight, even under laboratory conditions, that it is not an effective agent for control of schistosomiasis.

JONES and BRADY (p. 217) show that a (model) diatomaceous silica water filter was effective in preventing the passage of cercariae of *S. mansoni*.

S. japonicum.—A long and comprehensive report of *S. japonicum* infection in the Philippine Islands has been written by BANG and his colleagues (p. 435). They make the startling remark that it is possible for half the population to be infected and yet for the infection to be unrecognized by the local physicians. In their surveys they used a sedimentation technique for examination of faeces, and they claim that if this method [or presumably some other concentration method] is not used, a large proportion of infections will be overlooked. In hyperendemic areas 80 per cent. of children have enlarged livers, and the liver index is a useful guide to the prevalence of the disease. In Leyte, buffaloes and young pigs, and elsewhere rats, have been found infected. The only known snail host in the Philippines is *Oncomelania quadrasi*. American troops were infected in the course of engineering work associated with water, or while swimming or washing. For experimental work, guineapigs were found most suitable, and in therapeutic tests the efficacy of tartar emetic, Fouadin and anthiomaline was confirmed. Applications of benzyl benzoate or dimethyl phthalate to the skin affords some protection, and certain clothing materials commonly used in the U.S. army prevent penetration by cercariae, especially if the garments have been treated with benzyl benzoate, dibutyl phthalate, or a mixture of these.

WRIGHT *et al.* (p. 832) report on surveys made for schistosomiasis on Mindanao. Philippine Islands. PESIGAN (p. 1013) has found a focus of *S. japonicum* on Mindanao. *O. quadrasi* is present in canals and rice fields.

S. japonicum has been found in 11 districts of Szechwan, China, a province formerly regarded as relatively free ; KUO (p. 331) indicates that *Schistosomophora slateri* may be the snail host in some areas.

VOGEL (p. 330) has crossed *S. japonicum* with *S. mansoni* and a few of the resulting eggs produced embryos which developed in snails. The offspring resemble the female parent, and it is not certain that the process of reproduction is not one of parthenogenesis or pseudogamy.

The snail host of *S. japonicum* in the Philippines is *Oncomelania quadrasi*. MCMULLEN (p. 917) shows that this snail is amphibious and operculated, that it lives under varied conditions in scattered colonies, and that the main foci in which these snails come into contact with man are rice plots which have been abandoned for a time. He has observed the growth of these snails ; their life-span is at least one year and they may be infected shortly after hatching.

McMULLEN and GRAHAM (p. 917) think that, under war conditions, impregnated clothing and protective ointments offer considerable protection against cercariae of *S. japonicum*, but because no cercaricidal substance has yet been found effective in large bodies of water, practical control entails elimination of the snail host (*O. quadrasi*). Chemicals are best used against this amphibious species in the dry season. The authors tested 19 chemicals on plots of ground ; they were effective in killing the snails, in different concentrations, but all except two dinitro compounds injured the vegetation. Drainage and removal of the taller vegetation are also needed for the best results.

McMULLEN and INGALLS (p. 917) tested 10 chemicals against cercariae of *S. japonicum*. These had also been used in tests against *O. quadrasi*. Details should be sought in the original.

INGALLS (p. 442) has studied the action of salt water on the cercariae of *S. japonicum* ; sea water with 3 per cent. salt is lethal to cercariae within 3 minutes, but 1·5 per cent. is not, and such water is potentially dangerous to man, for instance where sea water is diluted by river water.

FAUST (p. 833) shows that eggs of *S. japonicum* (from the Philippines) may remain viable in the cold (at 4°C.) for 27 days if stored without washing, and up to 6 months if stored after washing. Winter temperatures in China and Japan are too low for hatching.

FAUST and INGALLS (p. 331) discuss the various techniques that have been used for examination of faeces for eggs of *S. japonicum*. They make the point that the zinc sulphate centrifugal floatation method is not satisfactory because only a small proportion of the eggs will float. Direct smear is useful, but sedimentation after homogenization in 0·5 per cent. glycerin in water, ether centrifugation, and the technique in which sodium sulphate solution, a detergent, and ether are used, with centrifugation, produce better results. The subject is discussed in detail, and readers should consult the original. HUNTER *et al.* (p. 440) also write in favour of the last method.

BAROODY and MOST (p. 333) find that if faeces are diluted with water and centrifuged, several times, examination of the sediment for eggs of *S. japonicum* gives more positive results than direct smear, and than the ether, zinc sulphate or brine floatation methods. This method has the additional advantage that it is simple.

HOLLANDS and PALMER (p. 439) have found that aspiration of the rectal crypts (even if normal in appearance), or scraping and aspiration of suspected lesions, is a valuable means of diagnosis of *S. japonicum* infection when faeces are negative. Aspiration is carried out with a motor-driven suction pump and a glass pipette, which are described.

An antigen consisting of a saline extract of cercariae of *S. mansoni* is not species-specific (though it shows a high degree of specificity for trematodes), and KATZIN and MOST (p. 440) have used it with success in an intradermal test for the diagnosis of *S. japonicum* infections. The tests became negative within 6 months in many persons who received Fouadin treatment ; they therefore have a value for prognosis.

WRIGHT *et al.* (p. 833) prepared antigens from adult *S. mansoni* for use in intradermal and flocculation tests for *S. japonicum* infection. The intradermal test gave somewhat disappointing results, especially in early cases, and only 83·7 per cent. of 104 persons microscopically diagnosed gave positive results with the flocculation test. Some non-specific reactions were observed.

WILLIAMS (p. 599) shows that a complement-fixation test, with an antigen prepared from livers of *Planorbis exustus* heavily infected with *S. spindale*, is outstandingly effective for the diagnosis of *S. japonicum* infections. The test is more sensitive and less tedious than repeated examination of the stools for ova.

She quotes the results, in 560 men examined, on which she bases her conclusions. DAKIN and CONNELLAN (p. 915) give an account of the outbreak referred to by Williams above, and report the same tests, but they also describe the symptoms, and the results of treatment with Fouadin, which were poor.

WINKENWERDER *et al.* (p. 834) report on 364 cases of *S. japonicum* infection in United States troops in the Philippines. The incubation period was from 26 to 58 days, and ova were found about one month after the onset of symptoms. Eosinophilia, often to 85 per cent. of the total leucocytes, was a common finding. Yellowish nodules were observed in the intestinal mucosa on sigmoidoscopic examination, and these were regarded as evidence of relapse after treatment. Fouadin, tartar emetic and anthiomaline were used in treatment; the relapse rate with Fouadin was about 40 per cent. MARTIN *et al.* (p. 334) note that a history of prolonged fever with urticaria, weakness, diarrhoea and other abdominal symptoms was the most significant clinical finding in American soldiers infected with *S. japonicum*.

LEAVITT and BECK (p. 916) make the point that *S. japonicum* infection was asymptomatic in a considerable number of members of an American hospital staff in the Philippine Islands. Diagnosis was made by examination of faeces and the recognition of small lesions (stellate distended venules, sometimes with a central pustule or ulcer) in the recto-sigmoid mucosa. Eggs were found in scrapings from these lesions.

MASON *et al.* (p. 732) report on American soldiers admitted to hospital some 6 months after the onset of acute symptoms of schistosomiasis. Early symptoms included fever and abdominal pain, sometimes with diarrhoea and palpable liver, rarely with urticaria and palpable spleen. Eosinophilia over 9 per cent. was common. Diagnosis during the later stage, by finding *S. japonicum* in the faeces, was rarely positive at the first attempt, and sometimes needed 10 or more examinations. Lesions detectable on proctoscopy were very rare. Eight of 481 patients showed neurological symptoms and two who were accidentally killed showed miliary abscesses in the liver. Treatment with potassium antimony tartrate (0·5 per cent.) gave better results than treatment with Fouadin.

TILLMAN (p. 600) discusses cerebral involvement in *S. japonicum* infection and reports 7 cases in which this diagnosis was made on clinical grounds. The symptoms are described; none of the patients (American soldiers) died, but treatment with antimony was only partly successful. WATSON *et al.* (p. 916) describe a case of cerebral involvement in *S. japonicum* infection; lesions in the brain were recognized at operation, the patient having had convulsive seizures, and localizing signs being present. CUTLER (p. 1079) also describes a case of *S. japonicum* infection in which the central nervous system was involved; treatment with Fouadin was very beneficial and the author advocates it, as early as possible.

Two cases of acute pulmonary lesions due to *S. japonicum* are described by WEINBERG and TILLINGHAST (p. 441); the radiographic appearances suggested miliary tuberculosis due, in one fatal case, to pseudo-tubercles which had formed around schistosome eggs. Cough, pain and scattered râles were present.

LIPPINCOTT *et al.* (p. 601), having made tests of liver function in *S. japonicum* infection, conclude that antimony treatment has a minor effect on the liver.

Other trematodes.—BERTRAND (p. 1080) reports a case of paragonimiasis from the Belgian Congo.

FEDERICO HEINERT (p. 1080) reports 26 cases of paragonimiasis from Ecaudor, discovered during the last 25 years. Most of the patients were cured by emetine.

DE OLIVEIRA and MEIRA (p. 668) diagnosed *Clonorchis sinensis* by examination of bile obtained by duodenal drainage, in a man born in Shanghai, who lived in Brazil.

FRIESS (p. 442) describes three cases of infestation with *Fasciola hepatica* in one family in Algeria; infection was probably acquired from watercress. Only one showed symptoms—loss of weight, slight fever, anorexia, anaemia and eosinophilia.

BONNE *et al.* (p. 1013) describe a new echinostome parasite of man in Java, *Echinostoma revolutum*, and discuss the probable snail hosts.

In Oregon, MACFARLANE and MACY (p. 97) describe a new species of cercaria (*C. oregonensis*) which causes swimmers' itch; the host snail is *Physa ampullacea*. The authors observed that the cercariae seemed to penetrate the skin as the water containing them evaporated; the dermatitis lasted from 1 to 4 weeks.

Cestodes

In a study of the life-cycle of *Diphyllobothrium mansoni* in Tonking, GALLIARD and NGU (p. 733) have found that three intermediate hosts (instead of two) are apparently necessary. The cycle is dog-*Cyclops*-tadpole-frog. Experiments to infect frogs by feeding them on infected *Cyclops* failed, but tadpoles could be so infected, and frogs could be infected by ingesting infected tadpoles. The authors therefore regard tadpoles as essential intermediate hosts.

A human case of sparganosis (undifferentiated) was reported, for the first time in the Belgian Congo, by FAIN (p. 1080).

Evidence is produced by VON BONSDORFF (p. 1081) that pernicious tapeworm anaemia (*Diphyllobothrium latum*) is due to interference by the worm with the interaction between intrinsic and extrinsic factors. The site of this interaction is probably the intestinal wall.

DICKMANN (p. 221) describes four cases of cysticercosis of the posterior cranial fossa.

NEGHME and FAIGUENBAUM (p. 734) have treated various forms of taeniasis with quinacrine, apparently with success.

A method for biological estimation of substances used in treating cestode infestations is described by HOLTON (p. 835).

VAN AMERONGEN (p. 734) notes that *Echinococcus granulosus* infection is common in dogs in the Dutch province of Gelderland, especially on farms where slaughter regulations are lax.

DUNGAL (p. 100) discusses the great reduction which has been made in the incidence of human hydatid disease in Iceland, where it was once very common. The decrease is ascribed largely to education of the people and to anthelmintic treatment of dogs each year.

In Egypt, EL KORDY (p. 601) shows that hydatid disease is common in camels (31 per cent.), buffaloes (16), cattle (10) and sheep (1·5 per cent.).

COLE (p. 602) describes the Australasian Hydatid Register, with 1,802 cases, almost equally from Australia and New Zealand. Most of the cysts were in the liver.

BRISOU (p. 222) has used, for the diagnosis of hydatid disease, extracts of tapeworms of different species, with which he performs intradermal tests. The active substance is a polysaccharide fraction joined to a distinct protein fraction, and it is about as specific as the antigen obtained from hydatid fluid. It is necessary to know if the patient has had tapeworm infestation previously. Details of preparation are given.

WATSON (p. 222) confirms a previous finding by STUNKARD that *Hymenolepis nana* is found in Syrian hamsters, but his investigations do not indicate that there is much danger of infestation of laboratory attendants who handle them.

HARANT *et al.* (p. 1013) found *Hymenolepis nana* in a child suffering from persistent diarrhoea, in Montpellier. Three other children in the same family were also found to be infected, and the authors report that almost half the population had suffered from persistent enterocolitis during the same summer. Infection had presumably been introduced by French African troops stationed there. *Charles Wilcocks*

[*To be continued*]

RABIES

JACOTOT, H. L'addition de latex d'*Hevea brasiliensis* au vaccin antirabique formolé en vue d'augmenter son activité. [**The Addition of the Latex of *Hevea brasiliensis* to Formolized Antirabic Vaccine as a means of increasing its Activity.**] *Ann. Inst. Pasteur.* 1948, Jan., v. 74, No. 1, 53–4.

The addition of a small amount of the latex of *Hevea brasiliensis* to antirabic vaccine prepared from formalized brain pulp increases appreciably the activity of the vaccine: results of experiments described indicate that only 9 of 57 guineapigs which received the vaccine containing the latex succumbed to the virulence test, compared with 34 out of 57 which received the vaccine without latex: in other words 84 per cent. of the first group, but only 40 per cent. of the second were protected. All of 19 non-vaccinated control guineapigs died.

These results are similar to those obtained when alumina gel was used as an adjuvant [see this *Bulletin*, 1948, v. 45, 291]. *H. J. O'D. Burke-Gaffney*

REMLINGER, P. & BAILLY, J. L'extension des vaccins antirabiques phéniqués et la nécessité d'une Conférence internationale de la rage. [**The Increasing Use of Phenolized Vaccines in Anti-Rabies Treatment and the Need for an International Conference on Rabies.**] *Bull. Acad. Nat. Méd.* 1948, v. 132, Nos. 9/10, 166–8.

In this paper communicated to the National Academy of Medicine in Paris at its meeting on 9th March, 1948, the authors again advance arguments in favour of the general adoption of phenolized killed virus vaccine for use in anti-rabies treatment.

Moreover they make a strong plea, based on the experience of French North African territories and elsewhere, not only for canine prophylaxis but also for the curative treatment of dogs and other domestic animals bitten by rabid animals.

In this connexion surprise is expressed that, by failure to recognize the greater utilitarian value of phenolized vaccines and the need for the vaccination of animals other than man, France has not kept abreast with modern ideas on anti-rabies treatment.

With a view, therefore, to having the whole subject of anti-rabies treatment reviewed and, if possible, uniformity of procedure reached, the authors urge the early calling of an international rabies conference, similar to that held in Paris in 1927. Items on the suggested agenda include: the nature of rabies virus; its culture; the influence of passage on the susceptibility of fixed virus to the action of attenuating agents; "*rage de laboratoire*" and paralytic accidents; rabies in the wolf and the intensive treatment necessary in the case of wolf bites; "failures" of treatment; criticism, particularly from the United States, of anti-rabies vaccination.

[The paper under review recapitulates the views expressed on anti-rabies treatment by the authors in their recent handbook *La Rage* ; see this *Bulletin*, 1948, v. 45, 387.] *G. Stuart*

MALARIA

SAUTET, J. A propos de la régression " spontanée " du paludisme. [**" Spontaneous " Regression of Malaria.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 1/2, 31–3.

As a result of observations in Corsica, the author in 1933 put forward the hypothesis that the so-called " spontaneous " epidemiological regression of malaria might be due to a limited tendency for the parasite concerned to form gametocytes, so that mosquitoes had less chance of becoming infected.

He now refers to an epidemic of malaria in Camargue in 1943, where endemicity of malaria is normally very low : in this outbreak, he was struck by the absence of gametocytes in the blood of those infected with the strain of *P. vivax*. This epidemic soon waned, giving place to the previously low endemicity.

These results contrasted strikingly with those found in intensely malarious areas in Corsica, where he had noted a gametocyte index of 26·3 per cent., or in the Lebanon where an index of 20 per cent. was found among Armenian refugees.

He refers to the results of SERGIEV and TIBURSKAYA [this *Bulletin*, 1945, v. 42, 622], who found that a strain of *P. vivax* from a southern region of the U.S.S.R. showed a greater tendency to produce gametocytes than did a strain from a northern region.

The author concludes that these findings support his thesis that the epidemiological regression of malaria is largely due to the limited capacity of the responsible strain to produce gametocytes. *H. J. O'D. Burke-Gaffney*

DOELEMAN, H. & VAN THIEL, P. H. De malaria-epidemie te Middelburg in de jaren 1940 tot en met 1945, benevens een onderzoek van parasietendragers. [**The Malaria Epidemic at Middleburg 1940–1945 and Parasite-Carriers.**] *Nederl. Tijdschr. v. Geneesk.* 1948, May 1, v. 92 (ii), No. 18, 1312–18. English summary (9 lines).

The report on this epidemic was given in full by DOELEMAN [this *Bulletin*, 1946, v. 43, 875] as a doctorate thesis. He concentrated attention on the parasite carrier, especially the healthy carrier, who makes little complaint of sickness, has a normal blood count and differential count and no alteration of his sedimentation rate. A few carriers showed lymphocytosis, but there was no indication of monocyte increase. These parasite-carriers were treated and 65 of them were very strictly under observation for at least a year. None of them had a relapse, either in the year or in the following year, showing that they still had the advantage of premunition. Confirmation was obtained of the assertion that the variation in the number of parasites was periodic, 10 to 16 days of a positive phase and 8 to 14 days of a negative phase. This was an important observation for the control of a parasite carrier. It was not necessary to examine the blood daily, but only 10 days and 16 days respectively after the previous examination.

That epidemic malaria occurred in Middleburg and nowhere else in Zeeland is explainable by : (1) the presence of parasite carriers ; (2) the incursion of parasite carriers ; and (3) conditions satisfactory for the maintenance of anophelines. The first of these explanations is the same as to state that

malaria is endemic in Middleburg : the second refers to the occupation of barracks by Germans, and the third to the presence of military horses in the centre of the town, so that more anophelines were attracted there than in normal years.

Now that Zeeland and Walcheren have been freed of malaria, responsibility that they shall continue to be free belongs to the medical practitioner. He should report all cases of malaria ; see that blood examinations are carried out and go carefully into the question whether the case is autochthonous.

W. F. Harvey

GARACI, C. L'andamento dell'infezione estivo-autunnale in Cassino. [**The Course of *P. falciparum* Infections in Cassino.**] *Riv. di Malariologia.* 1947, Dec., v. 26, No. 6, 283–95, 4 charts. [16 refs.] English summary.

The communes in the neighbourhood of Cassino were not malarious before the war, but after the destruction wrought by war in 1943 malaria became both prevalent and severe. The disease was widespread in 1944 ; *P. vivax* infections were most in evidence and only a few *P. falciparum* infections were identified. In the following year, however, *P. falciparum* became widely diffused and there were many fatalities. In July 1945, the Rome Institute of Malariology opened a diagnostic centre in Cassino and the results of some of their investigations are summarized in this report.

During the last six months of 1945, 2,312 blood samples were examined of which 58 per cent. were positive for malaria : of positive findings, 60·5 per cent. were *P. vivax* and 39·5 per cent. *P. falciparum.* In 1946, of 3,124 bloods examined, 66 per cent. were positive, *P. vivax* 86·1 per cent., *P. falciparum* 13·9 per cent.

P. falciparum infections rose in July and increases followed in August and September. The decline in the incidence curve commenced in October. In Central and South Italy, as a rule, the *P. falciparum* incidence curve rises steeply in July and August and thereafter declines almost as steeply. The July rise is hard to explain. In June, gametocyte carriers were very few ; the mean temperature was only about 21°C., at which temperature the extrinsic cycle of development of *P. falciparum* is of about a month's duration. It is hardly likely that the early cases were relapses of infections contracted in the previous year.

Norman White

HEISCH, R. B. **A Parasitological Survey of Taveta.** *East African Med. J.* 1948, Feb., v. 25, No. 2, 78–94, 5 figs.

This paper is a continuation of the author's parasitological surveys in Kenya Colony [this *Bulletin*, 1947, v. 44, 678] and refers to conditions in the small Taveta reserve, close to Kilimanjaro. Future workers will undoubtedly find these records of great value ; surveys in new countries today are so often handicapped by having no historical background. Also, a widespread sampling of the population and its environment is always likely to reveal something of immediate interest, and here the author has discovered a condition of splenomegaly which cannot be ascribed to any of the ordinary causes. The spleen rate of one group of adults living near Lake Jipe was 58 per cent. while the malaria parasite rate was only 18 per cent., a peculiar relationship for inhabitants exposed to hyperendemic malaria, where both rates should be low. This group showed, in addition, an 11 per cent. infection rate with the ova of *Schistosoma mansoni* on single stool examinations and it is suggested that the high adult spleen rate may be due partly to the presence of this helminth.

The malaria rates, as a whole, showed a wide degree of fluctuation, partly seasonal, but more probably due to the widely differing environments of forest, papyrus-covered lake, savannah, etc., and to the extraordinary medley of tribes which live there. Some of these tribes have always been exposed to hyperendemic malaria ; others, *e.g.*, the Wataita, have moved to Taveta from their relatively healthy highlands. The Wataita have, however, become adjusted to hyperendemic conditions quite well and although the crescent rate (of 22 per cent.) and the adult parasite rate (of 35 per cent.) were higher than the rates of the immune tribes, it was evident that they themselves had acquired quite a high degree of immunity. The author is unwilling to regard this as justification for the introduction of other susceptible tribes into Taveta and states that the introduction of non-immune immigrants would almost certainly be followed by a high initial mortality.

Haemoglobin estimations by the Sahli method gave figures varying between 50 and 70 per cent. in the younger children and about 80 per cent. in the older ones.

Plasmodium falciparum was the predominant parasite : *P. malariae* was also found, but no *P. vivax*. The vector anophelines were *A. gambiae* and *A. funestus*. *A. pharoensis* and *A. coustani* also were captured in large numbers in the author's tent. Larvae of *A. rivulorum* were found for the first time in this locality in Lake Jipe. Rice fields have recently been introduced into Taveta, but at present rainfall, rather than the flooding of the rice fields, is considered to be the more important factor in *Anopheles* breeding.

The presence of at least four potential mosquito vectors of yellow fever (*Aëdes aegypti, simpsoni, metallicus* and *taylori*) suggested that the disease might exist there in sylvan form. The blood of 10 monkeys, however, and of 15 human beings were negative for the mouse protection test.

Infections of *Schistosoma mansoni* were fairly widespread ; *S. haematobium* was restricted to a small village on the Tanganyika border. The molluscs were studied, but none could be incriminated as vectors.

A total of 185 stools were examined for helminths ; 40 per cent. showed *Ascaris* ova, less than 2 per cent. had *Ancylostoma*, and a few had *Taenia saginata*.

Ornithodorus moubata was present, but no relapsing fever was found. Children living in the forest showed a high infestation rate with the chigger flea ; this infection was absent in persons living outside the forest.

P. C. C. Garnham

TORRES CAÑAMARES, F. Nuevos datos sobre el *Anopheles marteri* Sen. y Pru. en España. Se trata de una variedad ? (Dipt. Cul.) [**New Data on *A. marteri* in Spain. Is it a Variety ?**] *Eos*. 1946, v. 22, Pt. 1–2, 47–58, 1 pl. & 5 figs. [11 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1948, Apr., v. 36, Pt. 4, 62.]

Comparison of the Anopheline found in Spain in the Provinces of Grenada and Cuenca and identified as *Anopheles marteri*, Sen. & Prun., with Senevet's descriptions and figures of this species has led the author to conclude that it is in reality a variety of it, which he describes from all stages as *A. marteri* var. *conquensis*, n. Characters distinguishing the adults and larvae of *A. marteri*, the new variety and *A. sogdianus*, Keshish'yan, which is also probably a variety of *A. marteri* are given in a table. The larvae of *A. m. conquensis* were usually found in clear mountain water, shaded and nearly still, often in association with *A. claviger*, Mg., and sometimes with *A. hispaniola*, Theo., or *A. maculipennis* var. *atroparvus*, van Thiel. In the laboratory, in water at a temperature of 20°C. [68°F.], only three examples out of 43 reached the adult stage ; the egg,

larval and pupal stages lasted 4–5, 39–51 and 4 days, respectively. The adults sheltered in damp, dark crevices in the ground or in masonry; they were seldom found in houses, but females were taken in June and February in a pig-sty. Of those taken in June, one contained undigested blood and another eggs; females containing eggs were found in the open country in June and September. Winter was passed in the adult stage; in October 1945, in intense cold, females were taken with a developed fat-body. *A. m. conquensis* is a mountain variety, occurring at altitudes of nearly 3,300 ft.

Patrissi, T. Epidemiologia della malaria e variazioni della fauna anofelica in rapporto alla bonifica del suolo. [**Epidemiology of Malaria and Variations in Anopheline Fauna in connexion with Land Reclamation.**] *Riv. di Malariologia*. 1946, v. 25, No. 2, 78–91. English summary. [Summary taken from *Rev. Applied. Entom.* Ser. B. 1948, Apr., v. 36, Pt. 4, 61.]

Following a discussion of the effects of land reclamation on the composition of an Anopheline population and the incidence of malaria, with special reference to work in Italy, and the effects of introducing fresh gametocyte carriers into an area of low endemicity, an account is given of investigations in 1941–42 in an area to the north of Venice comprising mainly reclaimed parts of the communes of Caorle, Portogruaro and Fossalta di Portogruaro. Malaria is endemic in the area, decreasing in intensity from the coast inland, and is practically absent from the third commune. Although most of the reclamation dates from 1922, there are still occasional outbreaks. The Anophelines taken were *Anopheles maculipennis*, Mg., vars. *typicus*, *messeae*, Flni., *melanoon*, Hackett, and *sacharovi*, Favr. (*elutus*, Edw.), and *A. claviger*, Mg. (*bifurcatus*, auct.). The incidence of malaria was lowest where the percentage of *A. m. sacharovi* was small. The salt content of the canal water ranged from 0·08 to 2·72 per cent.; larvae of *A. maculipennis* were found in several canals, those of var. *sacharovi* occurring in a few in Portogruaro in which the salt content was 2·47–2·72 per cent. Mosquitos were collected fortnightly from June to September in 1942 in houses and animal quarters, and the results are shown in a table. The density of var. *sacharovi* was not always greatest in the areas in which the water was most salt, but the percentage represented by it was lowest (1·2) in Fossalta, where there were no suitable breeding places, and it was concluded that these rare examples had immigrated from neighbouring districts. Precipitin tests showed that the percentage of the Anophelines that had fed on human blood ranged from 0·9 to 27·5 and tended to vary directly with the percentage of *A. m. sacharovi* present in the locality.

Buonomini, G. & Mariani, M. Qual'è il valore sistematico del nome *maculipennis* Meig. ? [**What is the Systematic Value of the Name *maculipennis*, Mg. ?**] *Riv. di Malariologia*. 1946, v. 25, Nos. 3/4, 101–7, 1 pl. English summary. [Summary taken from *Rev. Applied Entom.* Ser. B. 1948, Apr., v. 36, Pt. 4, 61–2.]

The authors discuss from their own investigations and the literature the morphological characters of the egg, larva and male hypopygium that have been used to distinguish the Palaearctic varieties of *Anopheles maculipennis*, Mg., and from the results of these, and of crossing experiments in the literature and differences in distribution and ecology, they distinguish three species [in contrast to Bates, who recognizes five]. These are *A. maculipennis*, including race *messeae*, Flni., egg varieties *melanoon*, Hackett, *fallax*, Roub., and *subalpinus*, Hackett & Lewis, and biotype *cambournaci*, Roub. & Treill.; *A. labranchiae*, Flni., including race *atroparvus*, van Thiel, and egg varieties *pergusae*,

Miss., and *sicaulti*, Roub. ; and *A. sacharovi*, Favr. The geographical distribution of the three species is shown on a map, and a new specific group within the subgenus *Anopheles*, named *Maculipennia*, is erected for them. The diagnostic characters of this group are described, and characters are given in a table distinguishing the three species in the egg, larval and adult stages (these last consisting mainly of differences in the male hypopygia), with notes on habits. A list of the Italian Anophelines is included.

YOUNG, M. D., HARDMAN, N. F., BURGESS, R. W., FROHNE, W. C. & SABROSKY, C. W. **The Infectivity of Native Malarias in South Carolina to *Anopheles quadrimaculatus*.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 303–11, 1 fig.

The susceptibility of anopheline mosquitoes to infection with the different species of malaria parasites has usually been worked out in the laboratory by means of artificial infections. In this investigation, natural infections were used and their infectiveness to the local anophelines (*A. quadrimaculatus*) was determined. The patients were negroes living in South Carolina and were known to have had malaria within recent months. A hundred mosquitoes were fed on each patient, irrespective of whether his blood contained gametocytes or not or even parasites of any sort : 14,811 mosquitoes were fed in 165 " lots "; 142 lots were fed upon *P. falciparum* patients ; 14 lots on *P. malariae* ; and 9 on *P. vivax*. The last were all negative (in fact at the time of feeding, only one case showed parasites and these were all asexual). The *P. malariae* cases showed gametocytes in four instances and three of them infected the mosquitoes. Twenty-five patients out of the 124 *P. falciparum* cases showed gametocytes, all in low density, and 16 of these infected mosquitoes. Some of the patients showed neither sexual nor asexual parasites at the time of feeding, and yet four of these cases were infective to mosquitoes. The patients without symptoms were just as efficient carriers as those with symptoms. The whole trend of these experiments shows that gametocyte density can be extremely low and yet mosquitoes can become infected under such conditions. The majority of the infections resulted from feeds on people showing fewer than 10 crescents per cmm. of blood. One patient with a *P. falciparum* infection was able to infect mosquitoes throughout a period of eight months. The duration of this species of infection appeared to approach a year, but further work is progressing to determine the exact duration. *P. C. C. Garnham*

WILLIS, E. R. **The Olfactory Responses of Female Mosquitoes.** *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 769–78, 2 figs. [13 refs.]

Anopheles quadrimaculatus and *Aëdes aegypti* were used in a series of experiments in an attempt to observe and record their olfactory responses. Most of this paper consists of a description of the olfactometer and the experimental technique and is not easily summarized.

A diagram is given of the apparatus through which two streams of air are passed ; either could carry an odour while the other served as a control. Light, temperature, humidity and other factors are regulated.

For each test, 50 female mosquitoes of known age were placed in a wire cage with a glass front, into which the two air streams arrived. Photographic records were made of the mosquitoes' movements at intervals of one minute for a test period of ten minutes. Counts were made on the developed films, which showed the numbers and distribution of the insects.

Data are presented which show that non-blood-fed females of both species were attracted by the odour of the human arm when the air was at 34°C. and

between 70 and 85 per cent. relative humidity. Blood-fed females of *Aëdes aegypti* and males are not attracted to arm odour. There was no indication that carbon dioxide in 1, 10 or 50 per cent. concentrations was attractive to either species. [See also this *Bulletin*, 1947, v. 44, 787]. *H. S. Leeson*

ROSENSTIEL, R. G. **Dispersion and Feeding Habits of** *Anopheles freeborni*. *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 795–800, 3 figs. [13 refs.]

One method of studying anopheline dispersion from breeding places is by marking, releasing and recovering female mosquitoes ; another is by measuring population fluctuations at successive distances from the breeding places. The latter method (adopted by the author) can only be used where breeding places are isolated. Two such breeding places were found in the Sacramento Valley ; one is referred to in this paper as the Dixon-Suisun area and the other as the Yuba City area.

The adult haunts chosen for study were those where *Anopheles freeborni* had been found the previous year. They were barns, basements, sheds, bridges and culverts which were situated at varying distances from the breeding places at intervals of a mile or two. They were visited once a week when mosquitoes were collected, counted and examined for eggs, fat body and species, then carefully returned alive to their resting places.

The two areas were divided into zones and the data recorded on charts. From these it is observed that no dispersal occurred until mid-July. Then there was a congregation of adults around the breeding places which went on until some time in the last three weeks in August, during which time the females were feeding. The numbers then declined about the breeding places and increased in the resting places up to five miles away, where there were no areas for breeding. During September and October dispersal was very active and was most noticeable within ten miles of the breeding places.

Adults from the Yuba area were found at least 4·5 miles to the south and some from the Dixon-Suisun area travelled at least 26 miles. Feeding went on during the dispersal and females contained eggs ; hibernating ones contained fat and those which managed to survive the winter were seen to contain eggs, fat or blood in the following February. *H. S. Leeson*

SILVA, W. Contribuição ao estudo da história da malária na cidade do Salvador—Bahia. [**A Contribution to the Study of the History of Malaria in the City of Salvador, Bahia.**] *Rev. Med.-Cirurg. Brasil.* 1945, v. 53, Nos. 2/3, 17–59, 5 graphs & 1 diagram. [56 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1948, Mar., v. 36, Pt. 3, 51–2.]

The author outlines the history and geography of Salvador, the capital of the State of Bahia, Brazil, in which malaria has been endemic, and occasionally epidemic, since it was first built. In 1929, *Anopheles argyritarsis*, R.-D., *A. albitarsis*, Arrib., and *A. aquasalis*, Curry (*tarsimaculatus*, auct.) were found to be common in the city. In 1936 a malarial service was instituted, the work of which included the inspection of dwelling-houses, the collection and identification of mosquito larvae and adults, and the preparation of blood smears. Tables and graphs are given showing data obtained in 1937–41 on the incidence of *Plasmodium falciparum* and *P. vivax* in persons of different age-groups ; on the death rate from malaria and other diseases ; on meteorological conditions and on the distribution of Anopheline breeding places. The larvae most commonly found were those of *A. aquasalis*, *A. argyritarsis*, *A. albitarsis*, *Aëdes scapularis*, Rond., and *Anopheles triannulatus*, Neiva & Pinto (*bachmanni*, Petrocchi), in that order. Adults of the first three species and of other

Anophelines were attracted to animal baits, but the only species taken in dwellings was *A. albitarsis*, and dissection of females of this species revealed sporozoites in the salivary glands and oöcysts on the stomach. The author concludes that well organised drainage and the regulation of streams are required to eliminate Anopheline breeding places, and shows in an appendix that the proportion of deaths due to malaria diminished as a result of the work done in 1939–41.

DE LUCENA, D. T. O *Anopheles* (*Nyssorhynchus*) *tarsimaculatus* Goeldi, 1905. Sua morphologia no Nordeste Brasileiro. [**The Morphology of** *Anopheles* (*Nyssorhynchus*) *tarsimaculatus* **Goeldi, 1905 in North East Brazil.**] Reprinted from *An. Soc. Biol. Pernambuco*. 1944, v. 5, No. 1, 7–13, 9 figs. on 6 pls. & 1 graph.

The English summary appended to the paper is as follows :—

" *Anopheles* (N.) *tarsimaculatus* Goeldi, 1905 is studied morphologically. Eggs, larvae and adults are described from material collected in the States of Alagôas, Pernambuco, Parahyba and Rio Grande do Norte.

" This is the first time that the species was found far from the coast (218 kilometers distant and more than 600 meters high), breeding in salt water, in the State of Pernambuco (Olho d'Ãgua dos Pombos).

" The finding of the species is in close dependence to epidemics of malaria."

DE LUCENA, D. T. Esbôço ecológico do *Anopheles* (N.) *tarsimaculatus* Goeldi, 1905 no Nordeste Brasileiro. [**The Ecology of** *Anopheles tarsimaculatus*, **Goeldi, 1905 in North-East Brazil.**] Reprinted from *An. Soc. Biol. Pernambuco*. 1946, v. 6, No. 1, 3–40, 4 maps & 2 graphs on pls. [29 refs.]

The English summary appended to the paper is as follows :—

" 1. *Anopheles tarsimaculatus* Goeldi, 1905 has been referred to as an anopheline mosquito breeding along the coastal plains, certain authors reporting it living some few miles inland, in this case breeding in fresh water.

" 2. This paper is an attempt to clarify some of its ecological habits. Geographical distribution is successively studied (*a*) in Neotropical Region ; (*b*) in Brazil and (*c*) particularly in Northeast of this country. Here the species was found in the Interior of the States of Pernambuco and Parahyba, respectively at distances of 255 kilometers at Olho d'Ãgua dos Pombos, and 115 kilometers at Queimadas, far from the coast.

" 3. Physiography and preference to certain areas in the referred States are emphasized. The species is in so close dependence to salt diluted in water of breeding places from Zones of ' Littoral ', ' Mata ' and ' Agreste ', that eggs oviposited by females captured in localities of high salinity rupture when layed in tap water. Besides sea water in coastal plains, rocks and soil provide salt for places where the mosquito breeds in the Interior. In João Pessoa, State of Parahyba, larvae of *Anopheles tarsimaculatus* were found in breeding places for fishes which water contained 33·345 grs. of salt per liter, while in Pernambuco, in the locality Russinha (' Agreste '), larvae breed in water until with 29·835 grs. of salt per litre.

" 4. Seventy six samples of water of breeding places were tested for Chlorides obtained from the Zones ' Littoral ', ' Mata ' and ' Agreste '. Results are shown in Table II. According to these data and a bibliographical revision it was possible to determine the zone of high salinity of Northeast that probably corresponds to the zone of *tarsimaculatus* incidence in the Interior.

" 5. The following adults habits were studied : (*a*) domesticity, (*b*) seasonal prevalence, (*c*) hour of penetration into houses. Zoophilic and anthropophilic habits were referred as well.

"6. *A. tarsimaculatus* was believed to be autochthonous in the Interior of Northeast States of Brazil : (*a*) because it breeds in salt water ; (*b*) it was found inland 252 kilometers distant from the sea ; (*c*) the water of streams, rivers, lakes and so on in this region always contains salt ; (*d*) geologically this is the most ancient region in South America."

NAIR, C. P. **Habits of Adult Anopheline Mosquitoes of Malaya.** Reprinted from *Med. J. Malaya.* 1947, Mar., v. 1, No. 3, 166–72.

Weekly night catches of anopheline mosquitoes were made from human habitations (3,912) and cattle sheds (5,073) in and around Klang, Malaya, from November 1945 to June 1946. Collections were made between 6 p.m. and 6 a.m. and fifteen species of *Anopheles* were obtained. Tables are given showing details of the catching stations and the numbers of times catches were made from them ; and the total number of each species for the whole period caught from human and animal quarters at 2-hourly intervals during the night. Seasonal fluctuations are not shown.

The numbers collected varied from 4,960 for *A. vagus*, the commonest species, down to 3 for *A. leucosphyrus*, the rarest. The figures show that *A. vagus*, *A. kochi*, *A. baezai* and *A. tessellatus* were more frequently caught in cattle sheds than in houses, and *A. separatus*, *A. barbirostris*, *A. umbrosus letifer*, *A. karwari* were more common in human dwellings. *A. hyrcanus sinensis* was equally common in both. Most species seemed to be active all night with a peak generally between 10 p.m. and 2 a.m. Other species collected were *A. maculatus*, *A. sundaicus*, *A. hyrcanus nigerrimus*, *A. philippinensis*, *A. subpictus* and *A. leucosphyrus*, but the numbers were so small that any general conclusions as to biting habits would be misleading. *H. S. Leeson*

CHWATT, L. J. **Infection of Reticulocytes by *Plasmodium falciparum* and *Plasmodium malariae* in Hyperendemic Indigenous Malaria.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 101–12, 8 figs. [24 refs.]

Previous work on the association of reticulocytes and malaria parasites showed fairly clearly that *P. vivax* had a marked tendency to invade reticulocytes, that *P. falciparum* was indifferent to the age of the cell and that *P. malariae* occurs almost exclusively in mature red blood cells. [See this *Bulletin*, 1935, v. 32, 423 ; 1939, v. 36, 495.] The present investigation was undertaken to discover which type of cell becomes infected in the long-standing infections associated with hyperendemic malaria. It was carried out on African children between the ages of 2–10 at Lagos, Nigeria.

The following method was employed to demonstrate reticulocytes and parasites. Slides were first prepared by allowing a drop of 1 per cent. brilliant Cresyl blue in 96 per cent. methyl alcohol to evaporate at one end of the slide. The blood was then mixed with this for 15 seconds and spread out in a thin smear, the drying of the blood being delayed by breathing on it. The film was then partially fixed by immersion for 1 minute in 20 per cent. methyl alcohol, and stained for 30 minutes in 1 : 20 Giemsa's stain in distilled water (*p*H 7·2).

Sixty-one cases were examined and records were made of the number of infected mature red blood cells, the number of infected reticulocytes, and the number of non-infected reticulocytes in 100 fields (or approximately 50,000 red blood cells). The minimum number of reticulocytes counted in *P. falciparum* infections was 1,000 ; in *P. malariae* 2,000. The results were compared graphically and statistically and showed that *P. falciparum* invades mature and immature cells indiscriminately, while the *P. malariae* is practically confined to mature cells. The degree of reticulocytosis varies according to the parasite

density. In uninfected children, the percentage is 2·4, in those with a low density it rises to 3·6, and in those heavily parasitized it may be over 12. The author concludes that persistent sub-clinical infections in African children are accompanied by increased erythropoiesis, the increase being related to the density of the infections. *P. C. C. Garnham*

CICCONARDI, A. & ALFANO, A. Sul reticolocitotropismo dei plasmodi nella malaria. Nota V.—Il diametro medio delle emazie mature e dei reticolociti durante l'accesso terzanario da Plasmodium vivax. [**Reticulocytotropism of Plasmodia. V. Diameter of Mature Erythrocytes and of Reticulocytes during *P. vivax* Infection.**] *Acta Med. Italica*. 1948, Jan., v. 3, No. 1, 13–17. English summary.

The authors have studied the blood cells during attacks of *P. vivax* infection. As regards uninfected cells it is possible to identify macro-erythrocytes and macro-reticulocytes. Infected cells gave an average diameter which is greater than that of uninfected cells. The average diameter of infected red cells is very near that of infected reticulocytes. *C. M. Wenyon*

ANDREWS, W. H. H. & MAEGRAITH, B. G. **The Pathogenesis of the Liver Lesion due to the Administration of Carbon Tetrachloride.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 95–100, 8 figs. on 2 pls. [30 refs.]

The effect on the liver of carbon tetrachloride, chloroform, and phenylhydrazine has been investigated in the course of experiments designed to elucidate the pathogenesis of the centrilobular changes found in malaria. Most of the experiments were made on rats, but other animals were also used. All the drugs produce central necrosis of the liver. The pathological changes are well-known, and are described briefly. In most species, the necrosis was accompanied by swelling of the parenchymal cells in the mid-zone, causing narrowing of the sinusoids. These vascular changes were investigated in greater detail by injection of Indian ink into the splanchnic system. In animals which had received carbon tetrachloride, the penetration of Indian ink into the liver lobules was much reduced.

In the discussion it is pointed out that poisons which cause central necrosis of the liver cannot do so by a direct toxic action on the liver cells, for in that case the cells most affected should be those first reached by the drug, at the periphery of the lobule. It is suggested that the necrosis is produced indirectly : swelling of the parenchymal cells obstructs the blood flow to the centre of the lobule, and the resultant anoxia leads to necrosis. It is not clear whether this swelling is a direct effect of the poison, or whether it also is a result of anoxia, caused by a reflex constriction of the blood-vessels. There may be other mechanisms causing central necrosis, since in some cases congestion and not constriction of the sinusoids is found after giving carbon tetrachloride.

[This paper should be read in conjunction with that of GLYNN and HIMSWORTH (*Clinical Science*, 1948, v. 6, 235) who injected Indian ink into the spleen of rats at varying intervals after a dose of carbon tetrachloride. They found the same impairment of penetration of the ink into the centrilobular sinusoids, and drew the same conclusions. These authors pointed out that both carbon tetrachloride and ligation of the blood vessels to the liver produce central necrosis, and in both cases there is a time-lag of 4–8 hours before the necrosis is fully developed. This is further evidence of a common factor in the two processes, which may be anoxia. They also observed that necrosis may occur in other conditions in which the liver cells are swollen, *e.g.* when they are loaded with fat.

Studies of this kind are clearly relevant to any discussion of the relation between interstitial tissue and parenchyma.] *J. C. Waterlow*

SCHNEIDER, T. **Haematemesis in Malaria.** *South African Med. J.* 1948, Apr. 24, v. 22, No. 8, 289–91.

This report concerns an African male of about 38 who was admitted to hospital in Johannesburg in May 1946 with headache and dizziness which had been present for a week, during which he had had one attack of unconsciousness and one attack of haematemesis. He had no history of gastric symptoms ; he had visited a malarial area the month before, but had no personal history of malaria.

On admission the patient had a temperature of 102·4°F. and looked ill, but examination revealed little of note, except the examination of the blood. This showed the haemoglobin to be 20 per cent., and the erythrocytes 1,140,000 per cmm. No malaria parasites were found. Despite daily slow transfusions of citrated blood, haematemesis and melaena occurred, the former being severe and persistent and being a daily feature. Hiccough appeared and became almost constant and the patient's condition was deteriorating. Ten days after admission, the erythrocytes were 1,430,000 per cmm. and the haemoglobin 24 per cent., and the anaemia was reflected in the blood picture. On this occasion, however, many *P. falciparum* parasites were found in the blood. Quinine bisulphate was given (10 grains, t.d.) and haematemesis stopped within 24 hours. Quinine was continued, the temperature fell to normal, and the haematemesis, melaena and hiccough disappeared. After a course of mepacrine, the patient made a good recovery and left hospital seven weeks after admission. An X-ray examination revealed no sign of gastric or duodenal ulceration.

A feature of the case was that the prothrombin index, bleeding time and clotting time were normal. The author compares this with other cases in the literature. The cause of the haematemesis is discussed and the author concludes that the condition was due to a toxic process leading to gastrostaxis initiated by the malarial parasite, since other causes would not be expected to result in so dramatic a response to quinine. Malaria should be considered as a possibility in cases of haematemesis coming from malarial areas.

H. J. O'D. Burke-Gaffney

PARAF, J. & LEWI, S. Réactions sérologiques faussement positives chez un paludéen anémique et ancien syphilitique. [**False Positive Serological Reactions in a Case of Malaria with a History of Syphilis.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1948, Nos. 12/13, 412–14.

Report of a case.

COATNEY, G. R., COOPER, W. C. & RUHE, D. S. **Studies in Human Malaria. VI. The Organization of a Program for testing Potential Antimalarial Drugs in Prisoner Volunteers.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 113–19, 1 fig.

In studies designed to test the comparative efficacy of drugs, old and new, in the treatment of malaria, an important contribution was made by white volunteer prisoners in the United States Penitentiary, Atlanta, Ga., who willingly underwent the discomforts and uncertainties both of malaria and of the experimental drugs. This paper describes the organization of these studies. One hundred and twenty volunteers were infected with malaria by the bites of infected *A. quadrimaculatus*. The St. Elizabeth strain of *P. vivax* was used to infect 105. The remainder were infected with the Chesson strain which

originated in New Guinea. The complete testing of a drug included a long-term protective test, a short-term protective test, and therapy during acute attacks of malaria. Observations were made on toxicity, and quantitative estimations of drug in plasma or whole blood were carried out. Observation of patients continued for 18 months after exposure to infection. *Norman White*

COATNEY, G. R., COOPER, W. C., RUHE, D. S., JOSEPHSON, E. S., YOUNG, M. D. & BURGESS, R. W. **Studies in Human Malaria. VII. The Protective and Therapeutic Action of Quinine Sulfate against St. Elizabeth Strain Vivax Malaria.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 120–34, 6 figs.

In the studies referred to above, quinine sulphate was the first drug used it was considered to be the logical standard of reference. Thirty volunteers were used in the protective tests. Each was exposed to the bites of 10 infected *A. quadrimaculatus*.

Quinine sulphate, 0·5 gm. daily for four days before infection, on the day of infection, and for 20 days thereafter, suppressed the early primary attack in all cases; primary attacks occurred after prolonged latent periods of 260 to 332 days. A dose of 0·25 gm. a day for the same period failed to suppress the early primary attack in four of five individuals.

Doses of 2·0 or of 0·5 gm. daily from the fourth day before to the sixth day after infection failed to suppress the early primary attack.

In the treatment of the acute attack doses of 2·0, 1·0 and 0·5 gm. daily for 6 days were used. Parasites disappeared and fever was controlled in all cases, the rate of action being roughly proportional to the dose used. Relapses occurred after intervals that were not influenced by the dose of quinine given in the treatment of the previous attack.

Toxic symptoms were frequent and at times severe: tinnitus, partial deafness, blurring of vision, nausea and vomiting, and urticaria, in that order of frequency, were noted. *Norman White*

YOUNG, M. D. & EYLES, D. E. **The Efficacy of Chloroquine, Quinacrine, Quinine and Totaquine in the Treatment of *Plasmodium malariae* Infections (Quartan Malaria).** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 23–8, 3 figs.

Fifty-four neurosyphilitic patients, both white and negro, were infected by the injection of blood containing *P. malariae*. When treatment started, 41 of these patients had experienced 15 or more febrile paroxysms; in some the infections had recently become asymptomatic but parasites persisted in the peripheral blood. The dosage of the drugs used was :—

Chloroquine, 0·6 gm. followed 6–8 hours later by 0·3 gm.; 2nd and 3rd days, 0·3 gm. in single dose each day. In some cases, the single daily 0·3 gm. doses were continued to, and including, the 6th day.

Quinacrine [mepacrine]: 0·1 gm. thrice daily for 5 days, or three doses the first day of 0·4, 0·3 and 0·3 gm., followed by 0·1 gm. thrice daily for 6 days.

Quinine: 0·67 gm. thrice daily for 4 days, then 0·67 gm. daily for several weeks.

Totaquine: 0·67 gm. thrice daily for 14 days.

A comparison was made of the rates of elimination of parasites under each of these treatments. Chloroquine gave the best results. Quinacrine was more effective than quinine. Totaquine gave the poorest results. *P. malariae* responded relatively slowly to all the drugs tested. Chloroquine eliminates *P. vivax* parasites much faster than *P. malariae* parasites from the blood even when the densities of *P. vivax* parasites are several times higher. There was

no evidence that increased amounts of acquired immunity accelerate the action of antimalarial drugs in clearing the blood stream from parasites.

Norman White

JAILER, J. W., ZUBROD, C. G., ROSENFELD, M. & SHANNON, J. A. **Effect of Acidosis and Anoxia on the Concentration of Quinacrine and Chloroquine in Blood.** *J. Pharm. & Exper. Therap.* 1948, Mar., v. 92, No. 3, 345–51. [13 refs.]

SHANNON *et al.* [this *Bulletin*, 1945, v. 42, 343] drew attention to the great variations in plasma levels of quinacrine (atebrin) in individuals on the same dosage schedule. Recently the same authors [this *Bulletin*, 1948, v. 45, 575] have indicated the effect on excretion of this and other drugs caused by oral administration of acid and alkali. The concentration of quinacrine in the tissues of animals was shown by MARSHALL & DEARBORN [this *Bulletin*, 1947, v. 44, 292] to be more constant than in plasma and there was a greater correlation with intake as well as with suppressive effect on avian malaria. In the present investigation, the acid-base balance of blood and its degree of oxygenation were evaluated as factors likely to influence the partition of quinacrine and chloroquine (a 4-amino-quinoline) between plasma and tissues. The drugs were administered daily to dogs in aqueous solution by stomach tube for periods of from 2 to 18 days and treatment ended 24 hours before experiment. Ten dogs received quinacrine and two chloroquine. During experiment the animal, suitably anaesthetized, was allowed to breathe air for a period followed by 10 per cent. CO_2 in oxygen to produce acidosis. Anoxia was achieved, after a period of normal breathing, by means of lowered oxygen tension as a result of re-breathing air from which CO_2 was absorbed. Gas analysis and *p*H measurements as well as estimation of drug levels were made on arterial blood, the last-named by the method of BRODIE & UDENFRIEND [this *Bulletin*, 1944, v. 41, 453]. CO_2 caused a doubling of the drug concentration in plasma and in red cells but no appreciable change in that of muscle or leucocytes. There was a return to normal during the recovery period when air was breathed. The blood during acidosis was fully oxygenated, but the *p*H dropped to 6·9 and CO_2 content rose steeply. Anoxia, on the other hand, caused no change in the drug concentration of red cells and plasma of dogs provided that the blood *p*H remained unaltered. The distribution of both drugs was high in tissue relative to plasma, and acidosis exerts its effect by altering the partition between the two. A considerable rise of concentration in the latter lowered only slightly that of the former. It appeared probable that the relative concentration of undissociated base is responsible for the distribution of drug between plasma and tissues.

J. D. Fulton

HALAWANI, A., BAZ, I. & MORKOS, F. **On the Antimalarial Activity of Nivaquine C.** *J. Roy. Egyptian Med. Ass.* 1947, Dec., v. 30, No. 12, 665–9.

Nivaquine C is 3-methyl-4 (diethylamino-pentyl) amino 7-chloroquinoline dihydrochloride. The powder is very soluble in water and absolute alcohol. Tablets of the drug contain 0·1 gm.

Nivaquine C is active against *P. praecox* in canaries and it is stated that in human malaria it is schizonticidal, but has a weaker action on gametocytes.

The authors quote DECOURT and SCHNEIDER [see this *Bulletin*, 1948, v. 45, 148] in Tunis as having treated adults with 0·3 gm. for 5 days, without any relapses after a year: but "the number of cases was not sufficient to allow of definite conclusions to be drawn".

The present authors investigated the antimalarial activity of Nivaquine C on 96 ambulatory patients at Khanka near Cairo. The patients were put on the following schedule :—

First day	...	3 tablets in the morning.
		2 tablets in the evening.
Second day	...	2 tablets in the morning.
		2 tablets in the evening.
Third day	...	2 tablets in the morning.
		1 tablet in the evening.

Fourth and fifth day, the same dosage as on the third day.

All infections were due to *P. vivax*, except one, which was a *P. falciparum* infection, in which rings and crescents were present : this patient did not complete the treatment.

In 46 cases, pyrexia and parasites disappeared after the first day of treatment. The remainder responded after 2 days. Gametocytes " required a few days more".

No toxic symptoms were observed. Only 9 patients relapsed, and a table compares these with the monthly incidence of malaria in the various villages concerned for three to five months. This average was about 12·2 per cent. compared with an average of 9·3 per cent. of relapses among 93 cases treated and followed up during the same period. It would appear that the incidence of malaria among those treated with Nivaquine was less than that in the general population of the villages in which they resided.

It is concluded that Nivaquine is a potent antimalarial drug which does not produce toxic effects in the doses suggested. It is mainly schizonticidal and gametocytes take a longer time than asexual forms to disappear after its use.

H. J. O'D. Burke-Gaffney

Singher, H. O., Millman, N. & Bosworth, Mary R. **Toxicity and Pharmacology of SN 13592. An Analogue of Phenyl Pantothenone.** *Proc. Soc. Exper. Biol. & Med.* 1948, Mar., v. 67, No. 3, 388–90, 2 figs.

" SN 13592 is characterized by an extremely low acute and chronic oral toxicity in several species. Local irritation effects are absent even upon repeated administration. Continued oral feeding of the drug induces an anemia which gradually disappears after the drug is withdrawn. Although there were no consistent effects on blood pressure and heart rate, a respiratory effect was noted. Smooth muscle was generally stimulated by this compound."

Burckhalter, J. H., Tendick, F. H., Jones, E. M., Jones, Patricia A., Holcomb, W. F. & Rawlins, A. L. **Aminoalkylphenols as Antimalarials. II. (Heterocyclic-amino)-α-amino-o-cresols. The Synthesis of Camoquin.** *J. Amer. Chem. Soc.* 1948, Apr., v. 70, No. 4, 1363–73.

Lutz, R. E. & Rowlett, R. J., Jr. **Antimalarials. 2,5-Diphenyl-3-furyl Amino Ketones and Alcohols.** *J. Amer. Chem. Soc.* 1948, Apr., v. 70, No. 4, 1359–63.

Yust, H. R. **DDT to control *Anopheles farauti* on Espiritu Santo, New Hebrides Islands.** *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 762–8, 1 fig.

Among the troops on Espiritu Santo and adjacent islands, there were over 400 primary malaria infections in January, 1943, and the same number for February. *Anopheles farauti* is the only anopheline on these islands and all stages are present at all seasons. An attack on this mosquito by the usual methods of control was started and by December 1943 primary infections were

down to 41 for the month ; for March 1944 the figure was 19. In April of that year DDT became available. Preliminary investigations showed that 10-minute catches in huts by two men averaged 73 *A. farauti* per hut. The DDT was first tested in cages and in the huts and then in July 1944 every hut and building was sprayed with 5 per cent. DDT in kerosene at the rate of 1 gallon per 1,000 square feet of surface, by means of a knapsack sprayer. In some cases, 10 per cent. DDT water suspension was applied by flit gun. This treatment was later extended to native huts and plantation buildings.

Larval control by weekly spraying of breeding places with 2 quarts or more per acre of 5 per cent. DDT in kerosene was done by hand sprayers, knapsack sprayers and by aeroplane.

No adult *A. farauti* was found during the rest of the year, and while in May, 1,456 larvae had been found in 38,701 dips, in October only 20 larvae were obtained in 42,525 dips. The average military strength during 1944 was just over 40,000 troops, but there were no primary malaria infections during November and December. *H. S. Leeson*

GALVÃO, A. L. A. & DAMASCENO, R. G. Alguns dados experimentais sôbre a ação do D.D.T. e do piretro contra o *Anopheles darlingi*. [**Experimental Study of DDT and Pyrethrum as Active Agents against** *Anopheles darlingi*.] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1947, July, v. 1, No. 2, 273–92, 3 figs. & 5 graphs. [11 refs.] English summary.

" 1. The *A. darlingi* mortality in a wood house treated with DDT dissolved in kerosene to give a final surface concentration of 2·09 gm. per square meter (195 mgr. per square foot) was determined. The mortality determined eight hours after contact was as follows :—One month post treatment, 97·3 per cent ; 2 months, 96·4 per cent ; 3 months, 92·1 per cent. ; 4 months, 95·3 per cent ; 5 months, 72·9 per cent ; 6 months, 67·7 per cent ; 7 months, 42·2 per cent. In the same period mortality observed in a control house was respectively, in per cent., 4·4 ; 3·9 ; 3·3 ; 10·4 ; 3·7 ; 4·5 ; 6·3.

" 2. The authors conclude that in houses of wood, residual film DDT may be applied at intervals of 4 months in climates in which there is no interruption in *A. darlingi* breeding or perhaps two times a year where winter interrupts breeding.

" 3. Captures in houses treated with DDT done with windows open and with windows shut showed no appreciable difference from the point of view of prophylaxis. This causes one to predict that this insecticide will be equally effective in the unprotected dwellings of our people in general.

" 4. The killing of adult mosquitoes with pyrethrum spray reduced their numbers very much on the nights on which it was applied but apparently this reduction did not reach a point where the transmission of malaria would be prevented.

" 5. The action of pyrethrum was not lasting with respect to *A. darlingi* since there was no considerable diminution in density on the nights subsequent to the spraying."

GARNHAM, P. C. C. **The Developmental Cycle of** *Hepatocystes* (*Plasmodium*) *kochi* **in the Monkey Host.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Mar., v. 41, No. 5, 601–16, 12 figs. (7 coloured) on 4 pls. [15 refs.]

In a preliminary paper [this *Bulletin*, 1947, v. 44, 882] the author gave a short account of the exoerythrocytic schizogony of *Plasmodium kochi* in the liver of monkeys. In the present paper he gives a more complete account of the developmental cycle of this parasite, which he designates *Hepatocystes*

kochi, adopting the name proposed by LEVADITI and SCHOEN in 1932 for the schizont stage in the liver of the baboon, which they did not connect with *P. kochi*. The blood forms of the parasite are all gametocytes, the youngest stage being a minute spot of chromatin with a tongue of cytoplasm in a red blood corpuscle. With growth a large amoeboid ring is formed. The cytoplasm then becomes irregular in shape, and finally, by a filling-in process, the spherical gametocyte is produced. The development of the gametocyte occupies 4 or 5 days. The mature gametocytes stain poorly in blood films. With Romanowsky stain the macrogametocyte takes a steely blue colour, while the less dense microgametocyte stains a biscuit colour. The pigment is in the form of very fine granules and at no stage does the red blood corpuscle show Schüffner's dots. The nucleus of the male gametocyte is a large oval-shaped pale pink area occupying a third to a half of the parasite. Scattered in the area are numerous deep red granules or threads of chromatin. The nucleus of the female gametocyte is much smaller and consists of a pale pink area with a dense mass of chromatin at the centre. Sometimes the single chromatin mass may be divided in two to six masses. The mature gametocytes appear to be extracellular and slightly larger than the normal red blood corpuscles. Attempts to infect clean monkeys by blood inoculation failed, though transference of gametocytes which appeared at once or later and persisted for periods up to 3 weeks took place. Exflagellation of the male gametocytes was easily observed. The infection in the monkey is very persistent and it is supposed that some of the merozoites from the liver schizonts must be asexual in character and able to give rise to fresh schizonts in the liver. The infected animals were not inconvenienced by their infection and showed no variations of temperature from the normal.

The schizogony in the liver has been described in the earlier paper. When a schizont is mature, merozoites are formed and these are scattered amongst the surrounding liver cells. They presumably find their way into red blood corpuscles to give rise to young gametocytes or into parenchyma cells of the liver to develop into schizonts. A liver cell is figured showing two undeveloped merozoites and two larger forms 4 and 5μ in diameter. In the section, each of these has peripheral nuclei. A similar but larger form 15μ in diameter is figured. As the parasite grows, the infected liver cell hypertrophies, the parasite becomes irregular in shape and vacuolated, while the nuclei multiply. Eventually the parasite assumes the form of a sponge with exterior prolongations and internal vacuoles. Finally the internal vacuoles coalesce, leaving an external band of cytoplasm with irregular processes extending among the liver cells, and a large central vacuole. The cytoplasm is filled with nuclei which eventually form the nuclei of the merozoites. In fixed tissues cut for sections, the cytoplasm in the mature cyst tends to shrink from the surrounding liver cells, appearing as a band of cytoplasm enclosing the large vacuole. When smears of the contents of a cyst are made, the cytoplasm breaks into fragments of various sizes and with Romanowsky stain they take a blue tint with red nuclei. In the early paper, these were described as cytomeres but it appears from sections that no definite cytomeres are formed. The mature cysts are referred to as merocysts. Attempts to produce infection in clean monkeys by inoculation with the contents of the mature cysts failed entirely.

The tissue phase of development of *P. kochi* is accompanied by highly characteristic cellular reaction. The parasitized hepatic cell hypertrophies enormously with repeated nuclear division. There is no tissue response till the parasite reaches 150μ or more. Then large numbers of polynuclear leucocytes accumulate and make their way in between the cytoplasmic processes. This may progress till all trace of parasite is lost, but in many cases the parasite continues its development. Then various cells of the lymphoid macrophage

system begin to accumulate between the parasite and liver parenchyma. There also appear large giant cells and phagocytic monocytes containing eosinophile granules. The parasite at this stage ruptures and its merozoites are scattered, while the remains of the parasite are invaded by the phagocytes. The site of the old schizont is represented on the liver by small fibrotic spots. Six mature schizonts gave average measurements of 1·8 by 1·3 mm.

Because of the peculiar character of the reproductive process with the production of the large spherical schizont with its central vacuole, the author believes that the parasite does not belong to the genus *Plasmodium*, nor does he agree with HAWKING and HUNT [this *Bulletin*, 1948, v. 45, 494] that it belongs to the genus *Haemoproteus*. He accordingly employs the name suggested by LEVADITI and SCHOEN (*C. R. Soc. Biol.*, 1932, v. 109, 343) naming the parasite *Hepatocystes kochi*.

The paper is illustrated by two coloured plates and two plates of photomicrographs. *C. M. Wenyon*

HAWKING, F., PERRY, W. L. M. & THURSTON, June P. **Tissue Forms of a Malaria Parasite** *Plasmodium cynomolgi*. *Lancet*. 1948, May 22, 783–9, 13 figs. (7 on 1 pl.). [18 refs.]

In an earlier paper HAWKING described pre-erythrocytic schizogony of *Plasmodium cynomolgi* in the liver of monkeys after he had been shown these forms by SHORTT, who had found them in monkeys infected by injection of sporozoites [this *Bulletin*, 1948, v. 45, 388]. The authors of the present paper give a fuller account of these experiments. They show that after the injection of sporozoites into monkeys the blood is infective to subinoculated monkeys for about 2 hours, after which it is non-infective for 7 days, 21 hours, when it again becomes infective. Study of the parasites which appear in the blood shows that the release of merozoites from the tissue forms is asynchronous and extends over three days. The number of parasites liberated varies from 1 million to 100 or 1,000 million, according to the infecting dose of sporozoites. The inoculation of emulsions of various organs of infected monkeys, including liver in which subsequent examination revealed pre-erythrocytic schizonts, failed to give rise to infections.

In sections of the liver of a 5-day monkey, the parasites measure on an average 12 by 14μ. They lie in enlarged liver cells, the nuclei of which are unchanged or slightly increased in size The chromatin masses in the parasite number about 70. In the liver of a 7-day 15-hour monkey, the average size of the parasite is $46 \times 31\mu$. The largest form found measured 68 by 61μ. In one cross-section there may be 100 to 250 masses of chromatin. Parasites very similar were found also in a 7-day 23-hour monkey. In most cases the parasites are roughly ovoid in shape, but sometimes they are quite irregular in outline and may show clefts in their cytoplasm or a tendency to segmentation into a number of separate masses which bear some resemblance to cytomeres. The host shows little tissue reaction to the presence of the parasite, but occasioually a parasite is invaded by polynuclear leucocytes. In one monkey inoculated intracerebrally with sporozoites, a form resembling a schizont was found in the brain. The paper is illustrated by twelve photomicrographs and a drawing showing variations in shape of a schizont in serial sections.

C. M. Wenyon

GRAMICCIA, G. & BLACK, R. H. **The Cultivation of Exoerythrocytic Forms of** *Plasmodium gallinaceum*. **I. A Preliminary Note.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 88–9, 2 figs. on 1 pl.

The method differs from that of HAWKING [this *Bulletin*, 1946, v. 43, 410] in that infected organs for tissue culture were obtained from birds which had

received intravenous inoculation of blood containing trophozoites of *P. gallinaceum*, instead of from birds which had been infected by sporozoites. Quinine (2·5 mgm.) was given daily until parasites appeared in the blood, when the dose was doubled.

Typical exo-erythrocytic forms were found in the macrophage-like cells on the eighth day of the culture. *P. C. C. Garnham*

CLARKE, Delphine H. & THEILER, M. **Studies on Parasite-Host Interplay between *Plasmodium gallinaceum* and the Chicken as influenced by Hydroxynaphthoquinones.** *J. Infect. Dis.* 1948, Mar.–Apr., v. 82, No. 2, 138–62, 5 figs. [40 refs.]

It is recognized that some drugs show different activity against the various stages in the developmental cycle of malarial parasites. A study of the action of 2-hydroxy-naphthoquinones on these different phases in *P. gallinaceum* infections of chickens is now reported with the object of elucidating some of the factors in the host and parasite which influence the activity of an antimalarial agent. The effect of the series of 2-hydroxy-naphthoquinones, synthesized by FIESER, on carbohydrate metabolism and respiration of erythrocytic forms of *P. knowlesi* and *P. lophurae*, was studied *in vitro* by WENDEL [this *Bulletin*, 1947, v. 44, 400].

The chemical constitution of the group differs from that of known antimalarials. In early observations on *P. gallinaceum* infections, it was found that they possessed activity against erythrocytic and exoerythrocytic forms and showed promise as prophylactic agents. The member of the group with which most of the present experiments were conducted was 2-hydroxy-3-β-decalyl-1 : 4-naphthoquinone, which occurs in a number of stereo-isomeric forms, each of which may differ in antimalarial activity. In some cases a mixture preponderating in *cis*-forms was used.

Infection was induced in young chickens by graded intravenous inoculations of infected *Aëdes aegypti* mosquito suspensions, prepared by grinding, or of parasitized blood, dosage being based on the size of the host. The course of the blood infection was followed in stained films and that of exoerythrocytic forms in smears of brain or by the method of COGGESHALL *et al.* [this *Bulletin*, 1945, v. 42, 699] as well as by subinoculation of fresh hosts. As a further test for sterilization of infection in an experimental bird the method of superinfection was used. Drugs were administered in the diet, in capsules or intramuscularly in suspensions of peanut oil and sometimes intravenously and the levels of the naphthoquinone were determined in plasma by spectrophotometric measurements on isoamyl alcoholic extracts of the highly coloured sodium salts.

When the drug was administered prophylactically, prior to sporozoite inoculation of chickens, parasites could not be detected in blood or brain smears by the methods outlined, in contrast to the results obtained with control or quinine-treated hosts. In subsequent experiments in which drug was given prior to sporozoite inoculation, in the prepatent and also in the patent period it was shown to be very active on the earliest phases of the developing parasite and was less active against the phase present four days after inoculation. By careful timing of drug administration, strong evidence was obtained that the effect was against the sporozoite itself, and complete prophylaxis was attainable. The naphthoquinone was also shown to be active against late exoerythrocytic forms of *P. gallinaceum*. Treatment of patent blood infections disturbed the synchronicity of the developmental cycle and growth was retarded.

Comparison of the activities of the naphthoquinone, quinine and atebrin (mepacrine) on blood induced infections showed that all three reduced the number

of parasites in the peripheral blood, but differences in their activity were obvious when inocula of various sizes were used, the naphthoquinone being generally the more active and there was a maximal inoculum which could be controlled by each drug. The development of immunity was believed to play an important part in the "cures" obtained. The level of drug in the plasma influenced the rate of response to treatment. Chronically infected birds showed greater immunity than those treated early in the infection. The immune state of the latter appears to offer further opportunities for studying the factors affecting latency, relapse and cure in this infection. Therapeutic treatment involves an interplay between parasite, host and the agent used. The results described here are in general agreement with those of GINGRICH *et al.* [this *Bulletin*, 1947, v. 44, 803] who reported cures in canaries infected with *P. cathemerium* on treatment with the same naphthoquinone. [This careful and extensive analysis of the factors which come into play during treatment of the different phases of a malarial infection merit consultation of the original article.] *J. D. Fulton*

See also p. 736, BLACK, **Leishman's Stain adapted for Use with Histological Sections.**

RIGDON, R. H. & MCCAIN, B. E. **Effect of 3,3′ Methylenebis (4 Hydroxycoumarin) "Dicumarol" on *P. lophurae* Infection in Ducks.** *J. National Malaria Soc.* 1948, Mar., v. 7, No. 1, 38–43, 2 figs.

When dicoumarin (3 : 3'-methylene-*bis*-4-hydroxycoumarin) was given in repeated doses by mouth to young white Peking ducks infected with *P. lophurae* it was found that the degree of parasitaemia was reduced in comparison with controls. The development of a peak of parasitaemia was also delayed and deaths occurred earlier in these treated birds. In a typical experiment with a group of 40 ducks about 3 weeks old, 10 were infected with *P. lophurae* and received no treatment, 15 were similarly infected and treated with dicoumarin, 15 others uninfected were given similar doses of the drug ranging from 25 to 100 mgm. on 5 to 7 occasions. Parasite counts were made in the usual way in stained films. In the control animals, anaemia, acidosis and haemorrhages in subcutaneous tissues were noted. Death appeared to be due to acidosis rather than anaemia and sometimes occurred rapidly in birds on low vitamin A intakes. The plasma was not coloured by haemoglobin, but its CO_2 combining power was reduced. The drug is obviously of no value in treatment and the mechanism by which it produced the above effects is not known.

J. D. Fulton

WALKER, H. A., STAUBER, L. A. & RICHARDSON, A. P. **Curative Action of Pamaquine Naphthoate, Quinacrine Hydrochloride, and Quinine Bisulphate in *Plasmodium cathemerium* Infections of the Duck.** *J. Infect. Dis.* 1948, Mar.–Apr., v. 82, No. 2, 187–96, 3 figs.

Screening tests for antimalarials were widely developed during the late war with the use of a number of different host species and parasites. While many drugs showed suppressive activity, cures were less readily obtained. Two reports of tests for curative action have been described by KELSEY *et al.* and by DEARBORN & MARSHALL [*Proc. Fed. Amer. Soc. Exp. Biol*, 1946, 185; this *Bulletin*, 1946, v. 43, 404] who used respectively *P. lophurae* infections of the chick and duck. The present authors now describe a curative test with *P. cathemerium* infections in the duck whereby certain drugs active in human malaria infections have been evaluated.

Peking ducks 10 to 12 days old of approximately 150 gm. were inoculated intravenously with 5×10^8 parasites per kgm. of body weight. At the peak of infection on the 4th day, 30 to 50 per cent. of the red cells were parasitized and by the 8th day parasites could not be found in thin films of peripheral blood of untreated fowls although it remained infective for fresh hosts over a period of some months. Different dosage schedules for each drug were used on 10 to 15 ducks one day before and for six days following inoculation. The drug-diet method or stomach tube was used for administration. A regular 3-hour dark and 3-hour light cycle was automatically maintained. Blood smears from each host were examined one day after the end of treatment and weekly thereafter till the 30th day from inoculation or on death of a bird. At the end of the observation period, fresh hosts were inoculated from the experimental birds and their blood was examined on alternate days for 15 days, a period regarded as suitable from other experimental observations. The donor birds were in turn inoculated with 5×10^8 parasites per kgm. of body weight and blood smears were made 3 days later and the nature of the resultant infection, if any, noted. Before a duck was regarded as cured, smears had to remain negative over the observation period, and the bird subinoculated from it had to remain free from infection. Finally the challenging dose to the donor bird had to give rise to a normal acute infection. Subinoculation and reinfection were regarded as a more accurate index of cure than absence of parasites in the treated birds. A few discrepancies were, however, encountered in these two criteria in so far as both might be positive or both negative. In all, 1,147 ducks were treated with different drugs and 269 satisfied all three criteria of cure. Pamaquin (plasmoquine) because of its properties was adopted as the standard in these experiments and effected a number of cures ; so also did quinacrine (atebrin), but not quinine. Results with 8-aminoquinolines other than pamaquin suggested a correlation between the present results and those recently obtained in man. *J. D. Fulton*

WALKER, H. A. & RICHARDSON, A. P. **Potentiation of the Curative Action of 8-Aminoquinolines and Naphthoquinones in Avian Malaria.** *J. National Malaria Soc.* 1948, Mar., v. 7, No. 1, 4–11.

Synergistic action between therapeutic agents of different chemical constitution against parasitic infections has frequently been noted. It is due possibly to the effect of these agents on different vital processes in the parasites. Such an action is now recorded in *P. cathemerium* infections of ducks between 8-amino-quinolines represented by plasmoquine (pamaquin) and pentaquine (SN 13,276) and three naphthoquinones (SN 5949, SN 12,320 and SN 13,936). Birds 10 to 12 days old weighing about 150 gm. were divided into groups of 10 to 20 and each was inoculated intravenously with 5×10^8 parasitized cells per kilo of body weight from a donor bird. Drug-diet therapy at different dosage levels was started 16 to 18 hours before inoculation and continued for 6 days thereafter. Examination of the host blood for parasites was made at intervals for several weeks after infection. Following blood examination 23 days after inoculation, each host was re-inoculated with the same number of parasites as in the first instance and blood smears were examined three days later. Absence of parasites during regular examinations after treatment was used as one criterion, and the other, which the authors consider more significant, was the attainment of a sufficiently high level of parasitaemia after reinoculation. It was shown that pamaquin, pentaquine and SN 12,320 given alone were curative, but the dosage required for 100 per cent. elimination of the infection was liable to produce fatal toxic effects. Pamaquin was more active than pentaquine, and showed about 20 times the activity of SN 12,320. Synergistic

effects were observed in various combinations of the two different types of drug in curative therapy, but were much less marked in suppressive therapy, suggesting that the mechanism in the two cases was different. From other experiments it appeared that SN 12,320 alone was more effective in the cure of well-established infections. The value of similar combinations to the above in the treatment of human malaria, as well as the mechanism by which the effect is produced, has yet to be determined. *J. D. Fulton*

TRYPANOSOMIASIS

Erratum

In the *Summary of Recent Abstracts, Trypanosomiasis*, this *Bulletin*, 1948, v. 45, at the foot of page 383, the following sentence "The author [van Hoof] thinks that melarsen oxide is useful for the treatment of patients with resistant strains (a conclusion not shared by Lourie)" does not correctly represent the views of Lourie, who shows, on p. 413 of the same issue, that he has confirmed van Hoof's findings The phrase in brackets, therefore, should be deleted.
Charles Wilcocks

Nash, T. A. M. **A Note on the Effect of High Temperature on the Pupal Stage of *Glossina* in relation to the Transmission-Rate of Trypanosomes.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 30–32.

In Burtt's experiments [this *Bulletin*, 1946, v. 43, 827; 1947, v. 44, 803] tsetse flies (*Glossina morsitans*) which hatched from pupae incubated at about 86°F. showed a greater transmission rate for *Trypanosoma rhodesiense* than those hatched from pupae kept at the lower average temperature of the laboratory. In Northern Nigeria, Nash [this *Bulletin*, 1942, v. 39, 532] found many pupae of *G. submorsitans* in soil at temperatures ranging from 69° to 82°F. but very few at higher temperatures, and as the shade temperature reached 106°F. (probably as high as anywhere in Africa) it is probable that Burtt's pupae were incubated at a higher temperature than they would experience in nature; his experiments should be repeated to compare the effect of temperatures of 68° and 82°F.

The author's work in Nigeria [see also this *Bulletin*, 1937, v. 34, 533; 1940, v. 37, 15] led him to conclude tentatively that most sleeping sickness conveyed by the riverine tsetse flies *G. palpalis* and *G. tachinoides* is contracted in the late dry season when the soil temperature is high and when the flies have become restricted to permanent water pools such as the village water holes; here contact between the flies and the people is close and the flies are compelled to feed largely on human beings. Confirmatory evidence for this view was not obtained from the dispensaries as the disease is mild in character and the people present themselves late for treatment. If it should be confirmed it may be possible to reduce the length (and cost) of protective clearings of river crossings to that required for the dry season only. *J. F. Corson*

Kleine, F. K. Unterschiede in der Bekämpfung der afrikanischen und der russischen Trypanosomiasis. [**Differences in the Control of African and Russian Trypanosomiasis.**] *Ztschr. f. d. Deut. Gesundheitswesen.* 1946, v. 1, No. 6, 143–4.

Domestic animals in southeastern Russia, where camels are much used in agriculture, are infected with surra (*Trypanosoma evansi*); as the trypanosome

is directly and mechanically carried from one animal to another by tabanid and other biting flies which do not themselves become infected, the control of surra would seem to be less difficult than that of those African trypanosomiases transmitted by tsetse flies which become infected and form an additional reservoir of the trypanosomes. The author refers briefly to the various well-known methods of controlling trypanosomiasis in man and animals.

As *T. evansi* and *T. brucei* resemble each other so closely in appearance it is thought that they are nearly related, but the former apparently cannot develop in tsetse flies; KUNERT and KRAUSE [this *Bulletin*, 1934, v. 31, 597; 1935, v. 32, 362] failed to infect *Glossina morsitans* with a strain of *T. evansi* isolated less than a year previously. [As was noted by the reviewer of their papers, the direct transmission of *T. evansi* by *G. morsitans* as late as the 3rd and 5th days after they had fed on an infected animal is remarkable; further experiments on direct transmission of pathogenic trypanosomes are desirable.]

J. F. Corson

KENEFORD, J. R., LOURIE, E. M., MORLEY, J. S., SIMPSON, J. C. E., WILLIAMSON, J. & WRIGHT, P. H. **Cinnoline Derivatives as Chemotherapeutic Agents for *Trypanosoma congolense* Infections.** [Correspondence.] *Nature*. 1948, Apr. 17, 603–4.

The authors have synthesized quaternary salts of various mono- and diamino-cinnolines, -quinazolines and -quinolines in which substituent amino groups can be more readily introduced than is the case with the more complex phenanthridinium compounds of the type described by BROWNING *et al.* [this *Bulletin*, 1938, v. 35, 344]. The latter compounds, especially "dimidium bromide" (1553) and "phenidium chloride" (897) are the most active substances so far described for the treatment of *T. congolense* infections of cattle in Africa. Two substances, 4 : 6-diamino-1-methylcinnolinium iodide and a derivative methylated in position 3 were found to be inactive against *T. congolense* infections in mice when pure, whereas the impure products of reduction had comparable activity to that of "897" but were much less active than "1553". The impurities in the two compounds were believed to arise from side reactions during reduction of the 6-nitro precursors and are possibly azo-compounds with symmetrical structures. Attention is drawn to the trypanocidal activity of certain other non-arsenical compounds with symmetrical molecules. Analogous activity of symmetrical sex hormones suggests that synthetic compounds with the type of structure suggested for the above active reduction products may provide useful trypanocides.

J. D. Fulton

WILSON, S. G. **Further Observations on the Curative Value of Dimidium Bromide (Phenanthridinium 1553) in *Trypanosoma congolense* Infections in Bovines in Uganda.** *J. Comp. Path. & Therap.* 1948, Apr., v. 58, No. 2, 94–106, 5 figs.

HARVEY, S. C. **Sulfhydryl and Disulfide Content of Normal and Arsenic-Resistant Trypanosomes.** *Proc. Soc. Exper. Biol. & Med.* 1948, Mar., v. 67, No. 3, 269–72. [12 refs.]

VOEGTLIN and co-workers [this *Bulletin*, 1924, v. 21, 414; 1925, v. 22, 142] showed that the —SH group was present in certain trypanosomes and suggested that tervalent arsenicals were capable of combining with it. Proteins with a similar grouping may also combine in the same way. The amount of the tripeptide glutathione, which in the reduced form contains the —SH group, was believed to play a part in the phenomenon of arsenic-resistance in trypanosomes. A quantitative estimation of sulphydryl and disulphide

groups (capable of yielding the former on reduction) in normal and arsenic-resistant strains of *T. equiperdum* and *T. hippicum* was therefore made, in order to test the truth of the above view. For this purpose, the trypanosomes were obtained free from red cells by centrifuging the blood of infected rats. The washed preparation was mixed with 15 per cent. trichloracetic acid and the solid obtained on centrifuging was resuspended and treated in the same way. The product was then suspended in dry acetone and shaken with the addition of a drop of concentrated HCl. After centrifuging the same process was repeated. On removal of the liquid *in vacuo*, the residue was ground to a fine powder and dried at 105°C. for 30 minutes. The method of MIRSKY and ANSON (*J. Gen. Physiol.*, 1935, v. 18, 307) was used for the estimation of —SH groups before and after reduction and the content of —S—S— groups present was obtained by difference. The values for the —SH groups present in normal and arsenic-resistant forms of both species of trypanosome showed differences which were not regarded as significant. The normal strain of *T. equiperdum* however contained an excess of disulphide groups compared with the resistant form, while in the case of *T. hippicum* the reverse was the case. There was no indication of a definite relationship between actual and potential —SH content of the trypanosomes and arsenic-resistance, and on this basis also no explanation was forthcoming why certain arsenicals with an acidic side chain are effective against arsenic resistant forms. *J. D. Fulton*

CHEN, G. & GEILING, E. M. K. **The Effect of Cysteine on the Antitrypanosome Activity of Antimonials.** *J. Infect. Dis.* 1948, Mar.–Apr., v. 82, No. 2, 131–2.

The authors [this *Bulletin*, 1945, v. 42, 869] showed that the trypanocidal activity and toxicity of trivalent, but not of pentavalent antimonials, for mice, was reduced by cysteine. The inhibitive effect of both types of compound on glucose metabolism of the trypanosomes was also antagonized by this substance *in vitro*. The effect on the trypanocidal activity of tartar emetic, sodium-antimony-thioglycollate, stibamine and neostibosan as judged by sugar metabolism *in vitro* has now been investigated by the methods previously described [this *Bulletin*, 1946, v. 43, 315]. Cysteine hydrochloride brought to *p*H 7·5 by trisodium phosphate was added to the trypanosome suspension at different intervals of time after the administration of the drug during the observation period of 1 hour. It was found that cysteine was able to antagonize the inhibitive effect of both the trivalent and pentavalent compounds on the glucose metabolism of *Trypanosoma equiperdum*. Experimental data in the case of stibamine indicated that there was a lag in the effect produced by this drug on trypanosome metabolism, in agreement with the delayed toxic effects produced by the same substance in mice compared with trivalent compounds. The possibility that the pentavalent antimonials exert their trypanocidal activity after reduction has frequently been suggested, but proof is still lacking. *J. D. Fulton*

CHEN, G. **The Effect of Methyl-Bis (β-Chloroethyl) Amine on** *Trypanosoma equiperdum*. *J. Infect. Dis.* 1948, Mar.–Apr., v. 82, No. 2, 133–7, 1 fig.

The effect of methyl-bis (β-chloroethyl)-amine (nitrogen mustard) on the glucose metabolism, morphology, motility, survival and reproductive powers *in vitro* of *T. equiperdum* has been investigated.

The effect of cysteine hydrochloride brought to *p*H 7·5 by trisodium phosphate was tested as an antagonist of the action of this drug. The methods for studying glucose metabolism have been described [this *Bulletin*, 1946, v. 43, 315]. After

the drug in suitable medium had been mixed with heparinized blood from an infected rat, the effect on reproduction was investigated by studying the number of dividing forms present in stained smears. Those with two parabasal bodies were put in this category. The infectivity for mice of trypanosomes kept in a concentration of the drug, which over a period of 1 hour did not produce any morphological changes, was also determined after centrifugation and replacement of the medium. The effect of the nitrogen mustard on the course of the infection in rats was also studied, but the substance proved very toxic for these animals. An inhibitive effect on glucose metabolism was shown by a 10^{-3} molar concentration of the drug, which is therefore less effective than tartar emetic or stibamine. With 5 times the above concentration, motility of the trypanosomes in suspension was impaired after 1 hour without significant reduction in numbers, and their morphology was at that time unaltered, but some change was evident after two hours. Dividing forms were reduced in number after exposure to a 5×10^{-4} molar concentration of the drug for 2 hours. The specific effect on the reproduction was shown by inoculating mice which had been subjected to different molar concentrations of the drug for 1 hour. From the increased survival time of the infected animals the minimal effective molar concentration of drug appeared to lie between 10^{-5} and 10^{-6}, while a maximal effect was produced at 10^{-3}. The mechanism of the effect on multiplication was studied by investigating the relationship between the dose of treated trypanosomes and the survival time. It appears that certain phases of mitosis are inhibited. Cysteine was able to antagonize the effect of the nitrogen mustard. *J. D. Fulton*

Malisoff. W. M. **The Action of the Endotoxin of *Trypanosoma cruzi* (KR) on Malignant Mouse Tumors.** *Science.* 1947, Dec. 12, 591–4, 2 figs.

LEISHMANIASIS

Ghosh, H. & Ghosh, N. N. **Complement-Fixation Reaction in Sera of Rabbits actively immunized with Living Culture of *Leishmania donovani*.** *Ann. Biochem. & Exper. Med.* Calcutta. 1947, v. 7, Nos. 1/4, 1–2.

—— & ——. **Agglutination Reaction in Sera of Rabbits immunized with different Strains of *Leishmania donovani*.** *Ibid.* 3–6. [12 refs.]

Three rabbits were immunized by intravenous injection of live cultures of *Leishmania donovani* given six times at intervals of four days. The dose of organisms was 100 million, increased to 1,000 million.

In the first paper, the titre of the complement-fixing antibodies is given as 1 in 8,000, 1 in 6,000 and 1 in 14,000. The complement fixation reaction was carried out with an emulsion of flagellates in 0·25 per cent. phenol in distilled water, the emulsion containing 80 million organisms per cc.

In the second paper, the agglutination reaction of the sera is described. Various antigens were prepared from culture flagellates. The titres of the immunized sera were 1 in 24,000, 1 in 16,000 and 1 in 32,000. There appears to be no " H " or " O " antigen in *Leishmania donovani*. *C. M. Wenyon*

Lubitz, J. M. **Pathology of Kala-Azar. Report of a Case.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 275–86, 8 figs. [11 refs.]

The author gives a short review of the pathology of kala azar and reports the autopsy findings in one case.

The subject was an East Indian seaman from Calcutta. Diagnosis was made by sternal puncture. A spleen puncture was also performed and the man died six hours later. The clinical aspects of this case have been reported previously [this *Bulletin*, 1947, v. 44, 986].

The abdominal cavity contained about 4,000 ml. of bloody fluid. There was a small round puncture hole on the convex surface of the spleen about 2·0 mm. in diameter. No blood clot or fibrinous deposit was seen on the capsule. The spleen weighed 1,030 grammes. The capsule was tense and the friable red pulp bulged above the cut surface. The liver was flabby and soft and the cut surface had a nutmeg appearance. There was a large area of broncho-pneumonia in the upper lobe of the right lung and scattered foci in the lower lobe. Small superficial ulcers surrounded by minute haemorrhages were noted in the rectum.

Microscopic examination of the spleen showed atrophic and scanty Malpighian follicles and highly cellular red pulp with enlarged and rounded reticular cells, some of which were parasitized. There were fatty changes in the liver parenchyma cells and hyperplasia of the Kupffer and interstitial cells ; parasites were seen in the latter. In the bone marrow there was increased cellularity, the bulk of which was " clasmocytic tissue " ; many leishmaniae were seen. Leishmaniae were not found in the lymph glands or in other organs and tissues.

In the brain, there was a " ring haemorrhage " in the basal ganglia and a small focus of gliosis in the pons. It was not decided whether these changes were due to kala azar or to some other conditions.

There are 7 good photomicrographs, and one photograph showing the cut surfaces of the liver and spleen. *L. E. Napier*

Cartwright, G. E., Chung, H. L. & Chang, A. **Studies on the Pancytopenia of Kala-Azar.** *Blood*. 1948, Mar., v. 3, No. 3, 249–75, 13 figs. [39 refs.]

The authors commence with a summary of the previous work on the blood picture in kala azar. The summary is a comprehensive one as far as work in China is concerned.

The present study is based on findings in 143 cases of kala azar diagnosed by the demonstration of *Leishmania donovani* ; of these, 27 were studied in great detail and the analysis of the findings in these cases forms the main body of this paper.

Anaemia was constant. The average haemoglobin for 124 uncomplicated cases was 8·3 grammes per cent. In one-third of the patients it was below 7 grammes per cent. The anaemia was significant (10·6 grammes), it occurred immediately after the onset of symptoms and was subsequently progressive. There was a positive correlation between splenic enlargement and anaemia.

The anaemia was normocytic orthochromic. Leucopenia was an almost constant feature of uncomplicated kala azar. The average white cell count of 124 patients was 2,835 per cmm. Only 16 patients had a white count above 5,000 per cmm. The leucopenia was apparent at the time of onset of the symptoms and it increased slightly in intensity with the progress of the disease. There was a correlation between a low white cell count and splenic enlargement.

The platelets were reduced in the majority of cases ; the average in uncomplicated cases was 103,000 per cmm. (330,000 being normal by this method). The thrombocytopenia developed later ; it was not usually present until two months after the onset of symptoms, but was progressive subsequently. In the presence of severe complications, *e.g.*, noma, the thrombocytopenia was more marked.

The bone marrow was always hyperplastic ; reticulo-endothelial cells constituted 5 to 50 per cent. of the total cells, but all the blood-forming cells were present, and the authors consider that the reticulo-endothelial proliferation is

mainly at the expense of the fat. The proportion of reticulo-endothelial cells tends to increase with the duration of the disease. One to 60 per cent. of the reticulo-endothelial cells were parasitized.

A table shows the bone-marrow differential counts in 27 cases. Polymorphonuclear leucocytes were reduced from the normal of 20 per cent. to a mean of 5·4 per cent. in the 18 uncomplicated cases. This change develops within the first month of the disease. The eosinophils were also markedly reduced ; they were often absent in a count of 500 to 1,000 cells. The erythroid cells were increased from a normal of 22 per cent. to 36 per cent. of all cells except reticulo-endothelial cells. The leucocyte-erythroid ratio is shifted from 3·5 : 1 to an average of 1·8 : 1.

The number of megakaryocytes was sometimes greater than normal, sometimes less : the average was slightly less than normal, *i.e.*, 122 per million nucleated cells, but platelet production was markedly reduced ; few clumps of platelets were to be seen in the marrow. In the treated cases, there was active platelet production and there were usually more masses of platelets than are seen in normal marrow, although in the peripheral blood the platelets were still short of normal.

The lymphocytes and monocytes were present in approximately normal numbers, but the plasma cells were somewhat increased.

During effective anti-leishmanial therapy, parasitized reticulo-endothelial cells disappeared and the percentage of reticulo-endothelial cells gradually diminished as the polymorphonuclear neutrophils increased. There was a significant increase in the eosinophilic cells. Lymphocytes became more numerous and the plasma cells diminished in number. Nucleated red cells became less numerous and the leucocyte-erythroid ratio returned to normal. At the same time the proportion of orthochromatic normoblasts to polychromatic normoblasts increased. The three cellular elements were restored to normal in the peripheral blood in the same order as their reduction from normal.

Evidence is presented which contradicts the view that the pancytopenia is due to a crowding out of the bone-marrow by reticulo-endothelial cells.

Certain similarities between the haematological changes in this disease and those accompanying the hypersplenic syndromes are noted. *L. E. Napier*

Sanchis Bayarri, V., Selfa, J. & Marco Ahuir, R. Formulas hematicas anormales en el kala-azar. [**Unusual Blood Findings in Kala Azar.**] *Med. Colonial.* Madrid. 1948, May 1, v. 11, No. 5, 363–8.

An account of two cases and a discussion on leucocytosis in kala azar.

Ho, E. A., Soong, T. H. & Li, Y. **Comparative Merits of Sternum, Spleen and Liver Punctures in the Study of Human Visceral Leishmaniasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Mar., v. 41, No. 5, 629–36.

In a series of 450 cases of kala azar, an attempt was made to appraise the value of the diagnostic methods, spleen, sternum and liver puncture, before treatment. Punctures were performed in other cases during and after treatment with urea stibamine.

The techniques are described shortly ; smears, stained by Wright's stain, were examined.

In a series of 450 cases finally diagnosed as kala azar in which spleen and liver punctures were performed before treatment, both punctures were positive in 375 (83·4 per cent.), spleen puncture only was positive in 64 (14·2 per cent.), and sternum puncture only was positive in 11 (2·4 per cent.). Among the

375 cases in which both punctures showed leishmania, larger numbers were shown in the spleen puncture material in 184 (49·1 per cent.) and in the sternum puncture material in 34 (9·1 per cent.).

In 121 cases of the same group, liver puncture was also done. Of these, in 118 (97·6 per cent.) spleen puncture was positive, in 108 (89·2 per cent.) sternal puncture was positive, and in 93 (76·9 per cent.) liver puncture was positive. In no instance was liver puncture alone positive.

In a series of 203 cases in which the punctures were performed during treatment, leishmania disappeared from both spleen and bone marrow at the same time in 138 (68·0 per cent.) instances ; in 41 (20·2 per cent.) instances the spleen puncture was negative while the sternum puncture was positive : and in 24 (11·8 per cent.) instances the reverse was the case.

In another 86 cases under treatment, parasites disappeared from the spleen, liver and sternum at the same time in 45 instances, while in the remaining cases they disappeared from the liver first.

After treatment, the " sternum and spleen punctures were found to check up each other very closely ".

The authors recommend that both spleen and sternum puncture should be performed to ensure accurate diagnosis. They consider that " once the technique is mastered, spleen puncture is the simplest of the three, but it is not so certain as sternum puncture, especially since the latter can be repeatedly tried without risk at one session ". [This statement is not understood.]

There were no ill-effects from the punctures performed in any of their cases.

L. E. Napier

TRINCÃO, C. **A New Reaction for the Diagnosis of Kala-Azar : a Preliminary Report.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 287–8.

While estimating iron in serum, the author noted that when 1 part of hydrochloric acid (0·3N) was added to 2 parts of serum of a kala azar patient, after a short interval the mixture became coagulated in a manner that reminded him " of the phenomenon demonstrated by the well-known formic aldehyde reaction of Napier ".

On addition of the hydrochloric acid there is " an immediate slight cloudiness . . . and, when the reaction is complete, the jellified serum may take on a darker tinge, its initial cloudiness is increased, and, though continuing translucent, it assumes a slightly milky appearance ".

The author tried this reaction in four other cases of kala azar, one in an advanced stage of treatment, the rest clinically cured. The first case gave jellification of the serum at the end of 24 hours and all produced a soft jelly.

The author has made hundreds of serum-iron determinations and in no other cases has the reaction occurred, except that in a case of multiple myeloma (aldehyde test=++) the serum jellified after 24 hours. *L. E. Napier*

SNOW, J. S., SATULSKY, E. M. & KEAN, B. H. **American Cutaneous Leishmaniasis. Report of Twelve Cases from the Canal Zone.** *Arch. Dermat. & Syph.* 1948, Jan., v. 57, No. 1, 90–101, 2 figs. [Refs. in footnotes.]

Cutaneous leishmaniasis is uncommon in the Panama Canal zone ; only 18 cases have been observed at the Gorgas Hospital since 1904. Of these, 6 were prior to 1937 ; the remaining 12 cases are included in this report. Very few cases have been reported in the Republic of Panama, outside the Canal zone ; two references to reports on 8 such cases are given.

In 9 of the 12 cases, the lesions appeared first in the dry season, January to March. All the patients were males. Six were soldiers from the United States

and three from Porto Rico. Three were labourers, 2 being Panamanians and one a Colombian.

"All patients had been in the Isthmus of Panama for several months before the appearance of the lesions, so that there is little doubt that they were autochthonous". The estimated incubation period was less than 2 weeks in 4 cases and less than a month in two others.

In nine cases there were single and in three multiple lesions.

The lesions were all on exposed parts of the body. All started as irritating "insect bites", which the patient scratched. All cases presented open ulcers, 0·5 to 9·0 cm. in diameter. The ulcers had raised sometimes undermined borders, with bases of granulation tissue; there was usually a copious thick serous discharge but occasionally a purulent discharge. "A striking feature was the occurrence of multiple small subcutaneous nodules along the regional lymphatics" in 5 of the 8 patients with lesions of the upper extremity. Most of these showed no inflammatory reaction. Regional lymphangitis and adenitis were also usual.

The histopathology is described in detail. It was noted that the cellular reaction in the subcutaneous nodules resembled closely that seen in the biopsy of the ulcers. Leishmania were found in the latter in each case, usually in macrophages but occasionally in epithelial cells, but were not found in the nodules. However, some treatment had been given in all the cases examined.

Treatment was by potassium antimony tartrate, Stibophen (Fouadin), or stibamine glucoside (Neostam), intravenously. Immediate (coughing, vomiting and chill) and late (joint pains) reactions occurred with all the drugs, but were most marked with potassium antimony tartrate. Improvement occurred within a week and the average healing time was 5·7 weeks. If the severity of the case was taken into consideration, there was little difference between the results obtained with the three drugs. *L. E. Napier*

PESSÔA, S. B. & ROTBERG, A. Nota sôbre o tratamento intensivo da leishmaniose tegumentar americana pelo tartarato de sódio e antimonila. [**Intensive Tartar Emetic Treatment of American Cutaneous Leishmaniasis.**] *Hospital.* Rio de Janeiro. 1947, Dec., v. 32, No. 6, 845–52, 10 figs.

The authors, following the experience of ALVES and BLAIR [this *Bulletin*, 1946, v. 43, 344] in the treatment of schistosomiasis by intensive administration of tartar emetic, have tested the method in six cases of S. American cutaneous or muco-cutaneous leishmaniasis. The solution used was put up in ampoules each containing 0·13 gm. of the salt in 10 cc. of normal saline with 5 per cent. glucose. Three ampoules were administered each day for two days, a total of 0·78 gm. being given in the six injections. In most cases the full course was repeated a second or a third time after three or four weeks. In some cases a modified course was given. The improvement noted in some of the cases would seem to justify further tests of this intensive treatment. *C. M. Wenyon*

FEVERS OF THE TYPHUS GROUP

MACCARTHY, Ethna. **Public Health Problems created by Louse Infestation.** *Irish J. Med. Sci.* 1948, Feb., 6th ser., No. 266, 65–78, 2 figs. & 4 maps. [14 refs.]

Among more than 5,500 persons coming from all the counties of Eire for the examination prescribed in the Health Embarkation Scheme for emigrants, high rates of louse infestation were found.

Among men, the percentage of infestation with body lice or their nits ranged from 30 to 65 per cent. in the different counties; for women the rates were considerably lower, but they refer only to the discovery of live lice and the real rate of infestation was believed to be as high as among the men. Head lice were found in 40 to 100 per cent. of the women from different counties.

Out of 401 persons tested by the Weil-Felix reaction, 154 reacted at 1–25 or over against *Proteus OXK*; against *P. OX19* and *P. OX2* the corresponding reactions were 33 and 37 respectively. The percentages of reactions among persons from "endemic" and "non-endemic" areas were much the same, except for the *P. OXK* reaction which was nearly three times more frequent in persons coming from the non-endemic areas.

A titre of 1–125 was reached in only 12 cases, in eight of which the reaction was with *P. OXK*; two reactions of this titre occurred with each of the other two strains, including one at 1–250 against *P.OX2*.

Two interesting family outbreaks of typhus are mentioned. One of these occurred in Drogheda in 1939 [this *Bulletin*, 1942, v. 39, 138], and it was found that every person attacked had engaged in unpacking trunks which contained clothing belonging to "old ladies who had been the sole survivors in their street of an epidemic in 1898". The other outbreak, in Galway in 1926, affected persons who in a search for firewood had broken into an old shack which had remained closed for 15 years since the death, in one day, from typhus fever, of a family of five. The shack contained only one bed. In neither outbreak was there any further spread of the disease and it appeared likely that the infection was caused by dust in which virulent rickettsiae had survived for periods of 41 and 15 years. *John W. D. Megaw*

GIROUD, P. & JADIN, J. Diagnostic différentiel des typhus par l'agglutination des rickettsies. [**The Differential Diagnosis of the Typhus Fevers by Rickettsia-Agglutination.** *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 1/2, 20–25.

The authors state in general terms their reasons for regarding the rickettsia-agglutination test as preferable in ordinary circumstances to the complicated complement-fixation test, as well as to the Weil-Felix and precipitin tests. They claim that the rickettsia-agglutination test of P. and M-L GIROUD easily differentiates between epidemic and murine typhus during the 3rd and 4th days of attacks and also after the height of the attacks. The difference between the epidemic and murine titres is less pronounced in the intermediate stage and also when the sera have been inactivated by heating or have been stored for long periods. *John W. D. Megaw*

HIRSZFELD, L. **Notes on New Methods in the Investigation of Typhus Fever.** *Texas Reports on Biol. & Med.* 1948, v. 6, No. 1, 21–2.

This work was begun during the German occupation of Warsaw and was temporarily discontinued in 1942, owing to the war.

The author isolated 30 strains of *Proteus X* from blood, urine and postmortem material of typhus patients with the use of Mueller-Kaufmann medium containing ox-bile. The best results were obtained from the inoculation of each tube of medium with 1 to 2 cc. of blood from the patient during the second week of the disease. A series of a dozen inoculations from each case is recommended. After 24 to 48 hours' incubation, transfer is made to agar. The strains isolated were agglutinated by the patients' sera in dilutions four times higher than was the case with a standard *Proteus X19* strain.

It was found that the sensitization of red cells influenced their absorption capacity on filter paper. This was applied, apparently with success, in the

cultivation of *Proteus X*. Serum from a typhus patient was added to his urine, which was filtered. Strips of the filter paper were then submerged in the Mueller Kaufmann medium and " in a large proportion of our cases Proteus X was cultivated."

During this investigation it was found that if patient's serum in decreasing amounts of 0·5, 0·4, 0·3, 0·2, 0·1 and 0·05 cc. was added to five tubes each containing 2·5 cc. of patient's urine, a precipitate was formed " in certain dilutions " after 15 minutes : but although this " uroprecipitation " test first seemed to be specific for typhus, it later gave positive results in typhoid and scarlet fevers and also certain anomalous results were found. The author suggests that if uroprecipitation indicates a specific substance, there might be also " another factor of overlapping antigenicity or an appearance in the urine of substance as a result of colloidoclasia ". [This paper is extremely brief and further confirmatory details of the results described would be required before a critical opinion could be offered on them.] *H. J. O'D. Burke-Gaffney*

BERCEANU, S. & CUCIUREANU, Iulia. Studiu asupra turburărilor nervoase din tifosul exantematic. Forme clinice speciale. [**Nervous Manifestations in Exanthematic Typhus ; Special Clinical Types.**] *Rev. Ştiintelor Med.* Bucharest. 1947, Nov.–Dec., v. 36, Nos. 11/12, 494–502. French summary.

During the course of an epidemic of typhus in Bucharest in 1943, 230 cases were examined by the authors. In 141 of these, nervous symptoms dominated the clinical picture. Confusion was observed in 55 cases, dysarthria in 15, deafness in 17, blindness in 1, strabismus in 1 and nystagmus in 2 cases ; 3 cases were bulbar and 16 meningeal in type. In all 230 cases there was some degree of cellular reaction in the cerebrospinal fluid. This was often slight in the presence of severe meningeal symptoms, and these cases formed a well-defined type of serous meningitis. A type was also seen where symptoms were predominantly those of compression due to cerebral oedema or increased pressure of the cerebrospinal fluid. These cases included 3 of hemiplegia and one with cerebellar symptoms. *D. J. Bauer*

HORTOPANU, D. Pronosticul tifosului exantematic. [**The Prognosis in Epidemic Typhus.**] *Rev. Ştiintelor Med.* Bucharest. 1947, Nov.–Dec., v. 36, Nos. 11/12, 510–21. [15 refs.] French summary.

Case mortality from epidemic typhus in Rumania has fallen considerably for several decades and in 1946 it was below 10 per cent., compared with 20 to 50 per cent. in the last century.

During the recent war, 465 cases were studied by the author, and he believes that this improvement is due, not to any epidemiological change as such, but to the better standards of life of the European populations, to progress in hospital organization and care of the sick, and markedly to the part played by sulphonamides and penicillin in reducing mortality attributable to complications.

Where nutritional and physiological states were low, as was seen among refugees and prisoners of war, the disease was of course more serious and the mortality higher : in " famine typhus " it has exceeded 20 per cent.

In a table, the author shows that a very important factor in causing death during typhus is the age of the patient. In his own records, 31 per cent. of deaths occurred in those over 40 years and 50 per cent. in those over 50. The exceptional gravity of typhus in those past middle age is stated to be due to existing arteriosclerotic lesions, which contribute to the serious complications

of the disease itself; this arteriosclerosis is localized in just those organs in which the acute local lesions of typhus are to be found, *e.g.*, the myocardium, brain and kidneys. The author, describing typhus as a "*maladie essentiellement artériolaire*", suggests that "the prognosis of epidemic typhus is inscribed on the patients arteries". He regards a rising blood urea as an important sign in diagnosis and prognosis.

The prominent sequelae of epidemic typhus, according to the author, are cerebral lesions, amputations for gangrene of the limbs, myocarditis and permanent mental disabilities; but in his experience such sequelae are not common and rarely exceed 1 per cent. *H. J. O'D. Burke-Gaffney*

ANIGSTEIN, L., WHITNEY, Dorothy M. & BENINSON, J. **Inhibition of Typhus and Spotted Fever in Guinea Pigs by Intradermal Inoculation of Antiorgan Sera and of certain Normal Sera.** *Texas Reports on Biol. & Med.* 1948, v. 6, No. 1, 87–96. [15 refs.]

The serum of rabbits which had been inoculated with the spleen and bone marrow of guineapigs contains antibodies against these organs, and is called antiorgan serum. An area of the skin of each of several guineapigs was infiltrated with this serum and after two hours the centre of the area was inoculated with brain substance of guineapigs infected with typhus and "spotted fever" [Rocky Mountain spotted fever.] Evidence of active infection was usually absent except for a few animals which suffered from greatly attenuated attacks. The serum of normal rabbits occasionally caused an attenuation of infection in guineapigs inoculated in similar conditions.

The interpretation of the barrier effect produced by the antiorgan serum is discussed and it is suggested that the production of a macrophage reaction by the serum may play an important part. The authors state that they can offer no suggestion as to the possibility of applying the results of their experiments to the prevention or treatment of typhus infections.

The original paper should be consulted by those interested in the problem of the protective action of antiorgan sera. *John W. D. Megaw*

ANIGSTEIN, L., WHITNEY, Dorothy & BENINSON, J. **Inhibition of Typhus and Spotted Fever by Intradermal Inoculation of Antiorgan or certain Normal Sera.** *Proc. Soc. Exper. Biol. & Med.* 1948, Jan., v. 67, No. 1, 73–4.

This is an abbreviated form of the above paper.

PLOTZ, H., BENNETT, B. L., WERTMAN, K., SNYDER, M. J. & GAULD, R. L. **The Serological Pattern in Typhus Fever. I. Epidemic.** *Amer. J. Hyg.* 1948, Mar., v. 47, No. 2, 150–65, 2 figs. [14 refs.]

This important paper contains the substance of four confidential reports submitted in 1944 to the Surgeon-General of the U.S.A. Army.

Most of the work described was done by Col. Harry Plotz, whose death in 1947 is deeply regretted.

A detailed study was made of serological reactions on sera collected every two days from 32 confirmed cases of epidemic typhus fever treated at Cairo in the winter of 1943. In attempts to recover rickettsiae from 23 of the patients, 21 strains of epidemic rickettsiae were isolated.

Strictly specific epidemic and murine antigens were prepared from yolk-sac rickettsial cultures by a modification of Craigie's method, in which the soluble non-specific antigens were removed by ether treatment combined with repeated

washing in saline of the rickettsiae deposited by centrifugation. The suspensions were preserved by the addition of formol to 0·2 per cent. Details of the technique employed are given in full for the first time.

The washed antigens gave no reactions with sera of patients or guineapigs convalescent from Q fever, Rocky Mountain spotted fever, boutonneuse fever, scrub typhus, and various other infections.

The antigens, after titration, were employed in a systematic series of complement-fixation and rickettsia-agglutination tests of which complete details are given in the paper.

The following extract from a table shows the average titres observed at various stages of the illness.

Day of Illness	Complement-Fixation (Epidemic antigen)	Rickettsia-Agglutination	
		(Epidemic antigen)	(Murine antigen)
2–5	0	10	0
6–7	5	40	10
8–9	20	320	80
18–19	640	10,240	1,280
28–30	320	2,560	640
61–90	80	640	80

Titres for the complement-fixation tests with murine antigen are not shown in the table, but from the complete data it appears that they were much lower than those with epidemic antigen, except in one case in which they remained the same till the 14th day on which both were 1–40.

Complement-fixing antibodies of epidemic typhus usually appeared about the 6th or 7th day ; in every case they were present before the 16th day.

Rickettsial agglutinins appeared earlier ; with epidemic antigens, no negative reactions were ever observed after the 7th day.

By both tests differentiation between epidemic and murine typhus was always possible ; the chief value of the agglutination test was the earlier appearance of positive reactions, but there was a greater degree of cross-reaction than with the complement-fixation test, with which in 18 cases the reaction against murine antigen remained negative throughout the illness, and in only four cases did the titres exceed 1–40.

With the Weil-Felix test (*OX19*) a titre of 1–80 was reached in 26 cases by the 8th day, and in the rest by the 11th day ; but, of course, the test did not help in differentiating epidemic from murine infection. *John W. D. Megaw*

Scoville, A. B., Jr., Bennett, B. L., Wertman, K. & Gauld, R. L. **The Serological Pattern in Typhus Fever. II. Murine.** *Amer. J. Hyg.* 1948, Mar., v. 47, No. 2, 166–76, 2 figs.

This paper is complementary to the preceding one : it contains the results of serological tests carried out in the same way on sera obtained from 15 patients during an outbreak of murine typhus in September, 1944, in Tennessee. Murine rickettsiae were isolated from eight of the patients.

The results obtained, *mutatis mutandis*, were generally similar to those reported in the preceding paper, except that the differential diagnosis between epidemic and murine typhus could not be made at so early a stage.

The murine rickettsia-agglutination reaction was still negative in four of the ten patients tested on the 8th and 9th days, but no negative reactions occurred after the 9th day.

The murine complement-fixation reaction with washed antigen was still negative in 12 cases in tests carried out on the following days of the illness :— 10th, 11th (3 cases), 13th (5 cases), 15th, 16th and 19th day.

With the non-specific soluble antigens the complement-fixation reactions became positive at an earlier stage in most cases.

The Weil-Felix (*OX19*) reaction was positive on or before the 7th day in all of the six cases in which early tests were made. No negative reactions occurred after the 9th day. The *OX2* reaction became positive considerably later or remained negative, the titres were always much lower than those with *OX19*.

The authors state that " Differentiation of epidemic and murine typhus fever can be made by complement-fixation or rickettsia-agglutination if highly purified antigens are used."

[If this statement implies that the differentiation can always be made by either of the two tests it seems to need qualification in view of the possibility that all strains of rickettsiae causing epidemic and murine infection may not give the same reactions as the strains dealt with by the authors. The delay in appearance of the specific complement-fixing antibodies is a drawback and it seems likely that the simple rickettsia-agglutination test with purified rickettsiae will hold the field as the best routine test for use in the differential diagnosis of the typhus fevers.]

This, and the preceding paper should be read and kept for reference by every worker on the serology of the typhus fevers. *John W. D. Megaw*

SOMAN, D. W. **A Study of Weil-Felix Reaction in the Diagnosis of Typhus Fever in Bombay.** *Indian Med. Gaz.* 1947, Nov., v. 82, No. 11, 649–53. [17 refs.]

The positive reactions observed in several groups of persons tested by the Weil-Felix method are summarized in the table which has been prepared from the material supplied in the paper.

Numbers of Positive Weil-Felix Reactions Observed.

	Proteus OX19			*Proteus OX2*			*Proteus OXK*		
	1–50	1–100 to 1–250	1–500 or over	1–50	1–100 to 1–250	1–500 or over	1–50	1–100 to 1–250	1–500 or over
500 sera sent for Wassermann test	1	3	0	0	0	0	1	0	0
763 sera from febrile patients including typhus cases	5	16	28	2	2	0	2	1	1
185 sera from enteric group cases	1	1	0	1	0	0	1	0	0
28 sera from typhus-group patients	0	1	22	1	10	1	0	2	2

It will be seen that there is no evidence of the occurrence of anamnestic rises in the Weil-Felix titre in cases of enteric-group fevers.

In 23 of the typhus-group cases the reaction was of the *OX19* type ; in eight of these, guineapig inoculation was carried out and *Rickettsia mooseri* is said to have been isolated from two of the patients : in four other cases the animals gave a febrile reaction and in two there was no reaction.

In two cases the reaction was of the *OX2* type ; serum from one of the patients was inoculated into a guineapig, with a negative result.

In three of the cases the reaction was of the *OXK* type and from each of the patients *Rickettsia orientalis* is said to have been isolated by mouse inoculation.

[The author, like most other observers in India, seems to regard it as axiomatic that the occurrence of a *Proteus OX19* type of agglutination indicates flea-borne murine typhus and excludes tick-borne typhus. PLOTZ *et al.* found that many cases of the tick-borne Rocky Mountain spotted fever gave an agglutination response of the *OX19* type, and that the complement-fixation test was needed to differentiate the disease from louse-borne and flea-borne typhus. (See, for example, this *Bulletin*, 1945, v. 42, 636.)] *John W. D. Megaw*

CALERO, C. **Outbreak of Typhus of the Murine Type. First Report from the Isthmus of Panama.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 313–21. [22 refs.]

Since 1932, sporadic cases of murine typhus have been diagnosed in the Isthmus of Panama at the average rate of three each year.

Between January 15 and February 5, 1947, there was an outbreak of 13 cases in the city of Panama. All the patients had worked in, or visited, a food store in which dead rats were found shortly after the occurrence of the first case. The cause of death of the rats was not ascertained.

Complement-fixation and rickettsia-agglutination tests strongly supported the diagnosis of murine typhus. *John W. D. Megaw*

RIGHTS, F. L. & SMADEL, J. E., assisted by Elizabeth B. JACKSON. **Studies on Scrub Typhus (Tsutsugamushi Disease). III. Heterogenicity of Strains of *R. tsutsugamushi* as demonstrated by Cross-Vaccination Studies.** *J. Exper. Med.* 1948, Apr. 1, v. 87, No. 4, 339–51. [28 refs.]

It has already been found that animals which have recovered from infection with one strain of *Rickettsia tsutsugamushi* [*orientalis*] are immune to all other strains of the organism, although striking differences have been shown to occur in the antigenic structure of the various strains when they are tested by complement-fixation, serum protection, and toxin-antitoxin tests.

In the present study, the authors have found that Swiss mice inoculated with vaccines made from the tissues of rats infected with various strains of *R. tsutsugamushi* usually became protected against homologous strains but often remained susceptible to infection with certain heterologous strains. Examples of the degree of protection conferred by vaccines of different strains are shown in the table.

Strains of Vaccines	Degree of Protection Conferred against Challenge Strains					
	Imphal	Karp	Kostival	Mite 21	Volner	Seerangayee (Malaya)
Imphal (India - Burma Border)	++	+	+	0	+−	0
Karp (New Guinea) ...	+	++	+	0	+	0
Kostival (New Guinea)	++	+	++	0	+−	0
Mite 21 (New Guinea)...	++	+−	+	+−	0	0

++ means "Immunity Index" 2·5 or above: + means Index 1·5 to 2·4: +− means Index 0·5 to 1·4: 0 means Index below 0·5.

Remarkable results obtained were :—(1) Vaccine made from Mite 21 strain gave little protection against infection with the same strain, but good protection against the Imphal strain, and (2) None of the four vaccines protected the mice against infection with the Seerangayee strain.

In spite of the obvious antigenic differences, the authors do not think it desirable to "indulge in taxonomic speculations regarding division of the subgenus *R. tsutsugamushi*".

The following comment is given in the authors' own words to illustrate the need for an agreed nomenclature of the typhus rickettsiae :—"It may be noted that while cross-immunity is exhibited by animals which recover from infection with *Rickettsia prowazeki* and *R. typhi*, or from infections with *Dermacentroxenus rickettsi* and *D. coroni*, nevertheless, vaccines prepared against one member of the pairs of agents afford comparatively little protection against the other". [Some readers are sure to be puzzled by the last three of these names which refer respectively to the rickettsiae of murine typhus, of Rocky Mountain spotted fever, and boutonneuse fever. "*R. coroni*" is, of course, a misprint for *R. conori*.] *John W. D. Megaw*

Dolgopol, Vera B. **Histologic Changes in Rickettsialpox.** *Amer. J. Path.* 1948, Jan., v. 24, No. 1, 119–33, 10 figs. on 4 pls.

A detailed description is given of the histology of the initial lesion, the maculo-papulo-vesicular rash, and a lymph node, as observed in biopsy material from patients suffering from rickettsialpox.

The initial lesion closely resembled the eschar of scrub typhus, both in its histology and naked-eye appearance, but it was more superficial and the vascular changes were less severe. Perivascular infiltrates were seen, but plasma cells were absent and mast cells were more numerous than in the eschar of scrub typhus.

The rash was similar in its microscopical features to that of other rickettsial diseases except that the cell infiltrates were much more profuse. The vascular changes were similar to, but less severe than, those of scrub typhus. The occurrence of vesicles in the spots is regarded as a unique feature of rickettsialpox among the rickettsial diseases.

The only evidence of damage to the lymph node was the presence of mast-cell infiltration of the lymphoid tissue ; there was no necrosis of the lymph node such as has been described as occurring in scrub typhus.

John W. D. Megaw

Kohls, G. M. & Parker, R. R. **Occurrence of the Brown Dog Tick in the Western States.** *J. Econom. Entom.* 1948, Feb., v. 41, No. 1, 102.

This note records the occurrence of *Rhipicephalus sanguineus* in four additional Western States of the U.S.A., namely Montana, Wyoming, Utah and Nevada.

H. J. O'D. Burke-Gaffney

YELLOW FEVER

Levi Castillo, R. Historia de la fiebre amarilla selvatica en America del sur en los primeros quince años (1932–1947). [**Jungle Yellow Fever in South America in the Period 1932–1947.**] *Kuba.* Habana. 1948, Feb., v. 4, No. 2, 37–42. [18 refs.]

[An account of much interest and useful for reference, but unfortunately not lending itself to abstract.] The author traces out year by year and notes

from a study of the records how rural and jungle yellow fever has spread from place to place (or been discovered in one place after another) or observed more widely in various parts of South America. In the Chanaan Valley first, thence to San Ramón in Bolivia and Caparrapí in Colombia ; the following year to Matto Grosso, next to Ecuador and much of São Paulo and other States, Minas Gerais, Paraná, Spirito Santo.

[Many of the references given are to papers and articles already abstracted in this *Bulletin*, and others have been abstracted to which the author does not refer.] *H. Harold Scott*

PLAGUE

WYNNE-GRIFFITH, G. **Pneumonic Plague in Rangoon.** *Lancet.* 1948, Apr. 24, 625–7. [25 refs.]

In Burma plague has long been endemic, and the same of course applies to Rangoon. Rangoon, however, has no record of a series of cases of pneumonic plague such as the present outbreak. It occurred in September and succeeded an earlier bubonic epidemic in spring. There were 16 deaths, but suspicions of the nature of the disease did not arise until the occurrence of case 11, which was the first notification to the health authorities. The epidemic had much the same course as other epidemics and much the same nature : high fatality rate and highly restricted area of diffusion. The epidemic rapidly burned itself out. An interesting point is raised in discussion : the assumption that pneumonic plague is very infectious. That assumption is questioned and, certainly in the present epidemic, the conclusion might be reached that " the disease is not particularly infectious ". Preventive measures are rightly to be taken in spite of the fact that " theoretically pneumonic plague is easily controlled ". The author continues :—" The incubation period is relatively short ; hence very few contacts will become cases after a week's quarantine. There is a distinct non-infectious phase lasting twenty-four to forty-eight hours after the onset of clinical illness . . . Immediate isolation during this phase of all cases of suspicious illness will effectively abort the outbreak ". *W. F. Harvey*

See also p. 708, TOMCSIK, Neuere Erfahrungen und Bestrebungen bei Cholera- und Pestimpfungen.

CHOLERA

KHALIL Bey, M. **The Defence of Egypt against Cholera in the Past, Present and Future.** *J. Roy. Egyptian Med. Ass.* 1947, Dec., v. 30, No. 12, 608–55. [12 refs.]

This address, which was delivered on 31st October 1947, was doubtless given to a special audience. It has particular interest at the present time as forecasting a possible or probable reappearance in May 1948 of the epidemic of cholera which has ravaged Egypt anew after a long interval of freedom. For the prevention of this danger, much evidently depends on the public health authorities. There are many details of historical interest set out very emphatically. Even more important than the views expressed as to the origin of the present epidemic, which follow current lines, is the declaration that reform is needed in the public health administration and the quarantine

administration of Egypt. The Egyptian Government has acted vigorously in providing funds for hygienic necessities. There is obvious need to provide a pure water supply from tube wells to three-quarters of the Egyptian villages, and the experience of the value of such a supply has been amply demonstrated in the present epidemic by the comparative immunity from cholera of urban populations provided with an urban type of water supply.

The old questions of the danger of the Mecca pilgrimage for Egypt according to the time of year at which it takes place are discussed. Evidently the institution of the quarantine station of El Tor has justified itself. It is now necessary, with air travel, to have a new convention to replace that of 1944; for the protection of Egypt is considered to be equivalent to the protection of Europe. *W. F. Harvey*

RAYNAL, J. H. Quelques mots sur le choléra en Egypte (automne 1947). [**A Note on the 1947 Cholera Epidemic in Egypt.**] *Méd. Trop.* Marseilles. 1947, Nov.–Dec., v. 7, No. 3, 470–74, 1 chart & 1 map.

KHALIL Bey, M. **The Effect of the Absolute Humidity of the Atmosphere on the First Wave of the Cholera Epidemic in Egypt in 1947.** *J. Roy. Egyptian Med. Ass.* 1948, Jan., v. 31, No. 1, 39–72, 9 charts & 1 map.

GOHAR, M. A. & MAKKAWI, M. **Some Observations on the Cholera Vibrio isolated from the 1947 Egyptian Epidemic.** *J. Roy. Egyptian Med. Ass.* 1947, Nov., v. 30, No. 11, 525–9.

"1. The morphology, cultural characters, resistance and pathogenicity of the Korain strain of cholera vibrio correspond to a large extent to those of the classical strains, except perhaps that the vibrio is not very markedly curved and rather short.

"2. Serologically it was found identical with the Inaba strain which is known to be the most prevalent strain in certain parts of India.

"3. Its short life inside dates is apparently due to the acidity produced by the fermentation of the carbohydrates present abundantly in them. Ten per cent. lemon juice is enough to kill it almost instantaneously."

GOHAR, M. A. & MAKKAWI, M. **Potassium Tellurite in the Isolation of the Cholera Vibrio.** *J. Roy. Egyptian Med. Ass.* 1947, Nov., v. 30, No. 11, 556–61.

The common enrichment method of isolation of the cholera vibrio by inoculation of stools in alkaline peptone water, incubation for 6 to 8 hours and then plating on alkaline agar may delay the isolation, or even render it more difficult than direct plating. Several experiments were undertaken to determine the meaning of this in terms of antibacterial action or overgrowth by other organisms, such as *Bact. alkaligenes*, *Bact. coli* and enterococcus. Antibacterial action was disproved and overgrowth incriminated. In fact the suggestion is made that it is the possession of an intestinal flora with the power of overgrowth that may determine infectivity for the individual.

The main endeavour was to find a selective bacteriostatic substance to incorporate in the nutrient medium, which would inhibit the growth of *Bact. alkaligenes* and *Bact. coli*, with less, or no, effect on the cholera vibrio. The substances tried were: potassium tellurite, potassium and sodium selenite, mercurochrome, methylene blue, thionin, basic fuchsin, brilliant green, crystal violet, neutral red, eosin and flavin. Of these, potassium tellurite proved the best when added to alkaline peptone water in a dilution as great as of 1 in 50,000. This has little effect on the cholera vibrio and the enterococcus, but has

bacteriostatic action on the other organisms. The enterococcus gave little trouble in the isolation of the cholera vibrio. Thus this method of enrichment " is recommended for the examination of convalescents, contacts, water and other suspected materials." *W. F. Harvey*

GOHAR, M. A. & MAKKAWI, M. **Cholera in Egypt. Laboratory Diagnosis and Protective Inoculation.** *J. Trop. Med. & Hyg.* 1948, May, v. 51, No. 5, 95–9.

One or two points regarding the recent outbreak of cholera in Egypt are brought out in this and the several papers which have appeared on the subject. It " created a state of terror almost amounting to panic ". The authors have devised a valuable method for reducing labour and saving time in the laboratory by eliminating the contaminating overgrowth of the " true " cholera vibrio by *Bact. alkaligenes*. This method has been described above [see also this *Bulletin*, 1948, v. 45, 600], and depends on the motility of the vibrio, its aerobic character and the inhibitive action of potassium tellurite. The " true " cholera vibrio is truly a highly selected organism.

A feat in mass vaccination was accomplished. " General vaccination of a population amounting to nearly 20 million people was achieved in Egypt probably for the first time in the history of this disease. One dose of 8,000 million organisms was given to everybody ; very few people received 2 doses ". As bacteriologists, the authors are cautious in their deductions. " It would be rash to try and draw any conclusion as to the value of general vaccination adopted in this epidemic ".

An extensive research was conducted into the viability of the cholera vibrio on various articles of food and clothing. A high correlation between the time of collection of dates and the time of occurrence of a cholera epidemic is commented on. *W. F. Harvey*

GOHAR, M. A. **A Rapid Method for the Bacteriological Diagnosis of Cholera.** *J. Roy. Egyptian Med. Ass.* 1947, Nov., v. 30, No. 11, 553–5, 1 fig.

[See this *Bulletin*, 1948, v. 45, 600.]

TANAMAL, S. J. W. Een Serologische en een colloid-chemische reactie ter onderscheiding van cholera-en El Tor-vibrionen. [**A Serological and Colloido-chemical Reaction for Cholera and El Tor Vibrios.**] *Nederl. Tijdschr. v. Geneesk.* 1948, May 8, v. 92 (ii), No. 19, 1370–75. English summary.

With the discovery of an El Tor vibrio strain in Celebes the El Tor question, as the author says, was infused with new life. Regulation tests for the true cholera vibrio were reviewed : haemolysin production—a bad guide ; exotoxin production—unsuitable in practice ; acetylmethylcarbinol formation—no differential value ; serum reactions—not distinctive. He is speaking especially of the differentiation of the haemolytic El Tor vibrio from the " true " cholera vibrio, and of antigenic analysis. This leads up to his introduction of a colloido-chemical test. A serum reaction is regarded as occurring in two phases, the first of fixation of antibody or " sensitization " and the second of flocculation by sodium chloride or saline as electrolyte. He has used as serum the Damang O-antiserum which is probably identical with the Hikojima or intermediate type. A number of electrolytes were tested and of these sodium carbonate Na_2CO_3, $2H_2O$ was the most suitable, while sodium bicarbonate was unsuitable. In this test a high-titre, disinfectant-free, cholera antiserum was diluted 1 in 200 with 0·3 per cent. sodium carbonate, and to it was added a concentrated vibrio

suspension in distilled water. The mixture is well shaken and it should be found that cholera vibrios remain consistently inagglutinable while El Tor vibrios flocculate completely and are deposited. If the soda solution is set up in series 0·1, 0·2, 0·3 . . . 1·0, 2·0, 5·0 per cent., it is found that up to 0·2 per cent. both vibrios flocculate out; above 0·2 per cent. only El Tor still flocculates, but above 0·5 per cent. the El Tor also remains in consistently stable suspension.

The second test depends on the replacement of the serum by chemical solutions alone: A few drops of concentrated vibrio suspension in distilled water are added now to the solution previously found unsuitable, namely, a 0·5 per cent. $NaHCO_3$, and after 15 minutes an equal volume of 0·5 per cent. mercuric chloride is added to the mixture. Now the phenomenon is reversed: cholera vibrios flocculate immediately, while El Tor vibrios remain in uniform suspension. *W. F. Harvey*

GREPPIN, J. Mission médicale suisse en Egypte. [**Swiss Medical Mission in Egypt.**] *Bull. Internat. Services de Santé des Armées.* Liège. 1948, Mar.–Apr., v. 21, Nos. 3/4, 53–61.

Switzerland through its Red Cross organization acted swiftly and philanthropically in offering its help to the Egyptian Red Crescent to control the outbreak of epidemic cholera. The offer was gratefully accepted and the party of doctors, technicians and hospital sister got to work at the small 25-bed hospital of Kafr-el-Zayat in the Delta region between Cairo and Alexandria. They found 186 patients in the hospital area. Patients commonly arrived comatose, dehydrated and cold. Treatment for shock consisted of the administration intravenously of 5 to 10 litres of glucose-saline in the 24 hours. Hypertonic saline or bicarbonate of soda solution were required for acidosis, while hypoproteinaemic patients received infusions of plasma.

The average case-mortality rate in this hospital has been calculated at 30 per cent., contrasting with that of Egypt generally, which was 50 per cent.

A laboratory was attached to the hospital, and although equipment was short much good work was done in isolating vibrios. A very active cholera phage was isolated, which caused lysis in the high dilution of 10^{-10} and was used to differentiate the Egyptian cholera strains from the El Tor vibrio and non-pathogenic strains.

Three villages and the population of Kafr-el-Zayat were treated with DDT, of which the Swiss had 1,000 kgm. of 50 per cent. powder. This was used in 2 per cent. aqueous suspension (1 per cent. of the active ingredient) for the walls of houses and sprayed by motor pumps under pressure of 20 atmospheres. Its lethal effect was observed not only on flies, but on lice, fleas, bugs, cockroaches, wasps and mosquitoes. The anticholera mission returned to Switzerland on 17th December. *W. F. Harvey*

HALAWANI, A. & OMAR, A. A. **Effect of Copper Sulphate on** *Vibrio cholerae.* *J. Roy. Egyptian Med. Ass.* 1947, Nov., v. 30, No. 11, 547–52.

"1. Copper sulphate is lethal in dilutions ranging from 20–45 parts per million to *Vibrio cholerae* in concentrations ranging from 10 to 1,000 million per cc. of Nile water.

"2. We believe that copper sulphate has its place in the prevention of cholera especially as it is used in this country in the eradication of snails in water canals."

Tomcsik, J. Neuere Erfahrungen und Bestrebungen bei Cholera- und Pestimpfungen. [**New Experiments and Discussion on Cholera and Plague Inoculations.**] *Acta Tropica*. Basle. 1948, v. 5, No. 1, 85–6.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

Billiottet. Le traitement d'assaut d'Hargreaves-Blanc dans l'amibiase intestinale. Un essai thérapeutique basé sur les mêmes principes. [**The Hargreaves Blanc Combined Treatment in Intestinal Amoebiasis.**] *Rev. Méd. Navale (Métropole et Outre-Mer)*. Paris. 1948, v. 3, No. 1, 101–8.

The author records his impressions of the treatment of intractable intestinal amoebiasis in a prison camp hospital in Saigon in 1945, and since. He considers that superinfection with a number of bacillary organisms aggravates the primary amoebic infection, and renders it refractory to specific anti-amoebic treatment. Dagenan, Septazine, or Rubiazol, the only sulphonamides available in the camp, produced spectacular improvement in refractory cases of intestinal amoebiasis. The dosages of these compounds compared favourably with that of sulphaguanidine necessary to produce a like result. Emetine and a sulphonamide concurrently are recommended as a routine in the treatment of intestinal amoebiasis.

In cases of failure with emetine and a sulphonamide, the combined " Hargreaves-Blanc " treatment with emetine, penicillin and sulphaguanidine, which gives excellent results, should be resorted to. *A. R. D. Adams*

Clampit, J. M. **Comparative Therapy of *Endamoeba histolytica* Infections in the Kitten.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 289–94. [13 refs.]

The author has used the kitten, which is not naturally infected with amoebae, as experimental host for comparison of the therapeutic effects of diodoquin, vioform, chiniofon, carbarsone and emetine on infections with *E. histolytica*. The disease in this animal runs a very acute course with ulceration of the colon and bloody diarrhoea ; control animals survived on average only three days after appearance of amoebae in the stool. Bacterial infections of the respiratory tract and eyes, anorexia and general malaise were common. Bronchopneumonia was the chief cause of death. In spite of the important fact that emetine has no action on amoebic infections of the kitten, as previously shown by Dale & Dobell [this *Bulletin*, 1918, v. 11, 248], the author considered it the most suitable animal for the tests. He states that —" the amebicides in present clinical use have never been comparatively assayed in an experimental animal using the same strain of *E. histolytica* under identical conditions, although all have known amebicidal activity "—and must therefore be unfamiliar with the work of Jones [this *Bulletin*, 1947, v. 44, 1069] who tested the therapeutic action of the above amoebicides in rats, with the exception that stovarsol replaced vioform.

Groups of 18 to 40 kittens weighing 350–650 gm., which appeared to be equally susceptible, were inoculated after laparotomy just above the ileo-caecal valve, with 5 ml. of culture material from egg-infusion medium, containing approximately 1 million amoebae per ml., and at the same time the colon was slightly injured by pinching with forceps. On the third day after operation, material obtained from the caecum or colon by rubber catheter was examined in fresh preparations, and was also cultured. Examinations were continued thrice weekly till the end of the experiment. Treatment was started when smear or culture was positive. The criteria

of cure were the absence of amoebae three weeks after the end of treatment or absence of amoebae or ulceration if death occurred during treatment. Emetine was given subcutaneously and the other drugs as a pellet in carbowax [composition not stated], which is stated to dissolve readily in the stomach. The dose in each case was based on that given to adult human cases. Only one kitten relapsed after negative smears and cultures and was apparently cured by courses of different amoebicides. Histological examination of various organs revealed few pathological effects from the drugs. They all showed activity in varying degrees, except emetine which was ineffective and no kitten survived more than seven days of treatment with this substance. *J. D. Fulton*

Noble, E. R. **Cell Division in** *Entamoeba gingivalis*. *Univ. California Publ. Zoöl.* 1947, v. 53, No. 7, 263–79, 41 figs. on 4 pls. [16 refs.]

Koppisch, E. & Wilking, Virginia N. **Balantidial Dysentery. Report of Four Cases with Postmortem Study.** *Puerto Rico J. Pub. Health & Trop. Med.* 1947, Dec., v. 23, No. 2, 185–224, 18 figs. [Refs. in footnotes.] [Spanish version 225–46.]

The authors review the literature dealing with balantidiasis and note the scarcity of detailed pathological studies on balantidial dysentery. They accordingly record their findings in four fatal cases of balantidial infection, three of which were acute cases of balantidial dysentery and one a chronic case. In two of the cases, the lower portion of the ileum was involved and in both of these perforation had occurred. In the acute cases the condition was characterized by total involvement of the colon in multiple and diffuse ulceration and extensive gangrene of the mucosa extending in some segments to all the coats. In the chronic case there were six small ulcers in the colon, and death was due to tuberculosis. Histologically the reaction showed infiltration with lymphocytes, plasma cells and monocytes invoked by the tissue necrosis rather than by the balantidia or the bacterial invaders. The paper is illustrated by 18 microphotographs in which the tissue reaction and invasion of the walls of the ileum, appendix and colon with balantidia are shown. *C. M. Wenyon*

Logan, J. L. **Human Coccidiosis.** *New Zealand Med. J.* 1946, Aug., v. 45, No. 248, 309–11.

Four cases of *Isospora hominis* were found among 5,286 examinations of service personnel.

RELAPSING FEVER AND OTHER SPIROCHAETOSES

Coghill, N. F. & Gambles, R. M. **Discussion of Methods for differentiating Tick- from Louse-borne Relapsing Fever Spirochaetes.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 113–17. [37 refs.]

The authors review in some detail the literature relating to the susceptibility of the guineapig to the various strains of human relapsing fever spirochaetes. These spirochaetes fall into two groups, the louse-borne strains (*Trep. recurrentis*) which are incapable of infecting guineapigs and the tick-borne strains which usually cause an infection in these animals.

The louse-borne spirochaete behaves in a remarkably constant way in this respect—it always gives a negative result on inoculation, so that the implication is that a strain is definitely tick-borne if it is able to infect guineapigs. This tick-borne infection, however, may be cryptic and may only be detectable by

sub-inoculation of the guineapig's blood or brain into a rat or mouse. The tick-borne spirochaetes vary in their receptivity to the guineapig. *Sp. hispanicum* (*sic*) of North Africa always produces a patent infection. The South American strains—*Sp.* [*Trep.*] *venezuelensis* and *Sp.* [*Trep.*] *neotropicalis* are completely refractory. It is concluded that the susceptibility of the guineapig provides a good biological test. [This test would be of little value in tropical Africa, where the reviewer and his co-workers [this *Bulletin*, 1948, v. 45, 86] showed that both types of spirochaetes were occasionally able to infect guineapigs. A better method of differentiating these African strains is to observe their behaviour (*a*) in monkeys (*duttoni* is fatal, *recurrentis* is not) and (*b*) in mice (*duttoni* causes persistent infections, *recurrentis* lasts for 2 or 3 days only).] *P. C. C. Garnham*

Constantinescu, G. & Ionescu, R. Contribuţiuni la studiul formei meningeale in febra recurentă. [**Observations on the Meningeal Form of Relapsing Fever.**] *Rev. Ştiintelor Med.* Bucharest. 1947, Nov.–Dec., v. 36, Nos. 11/12, 503–6. French summary (4 lines).

Of 295 cases of relapsing fever studied in 1945, 12 were of a meningitic type. The cerebrospinal fluid was usually clear, and not under pressure, and sometimes showed xanthochromia or gross haemorrhage. In no case could the causative organism be demonstrated in the cerebrospinal fluid. Meningeal signs appeared at the first onset of fever. They cleared up during the apyrexial period and did not reappear during the next onset of fever. The nervous symptoms were unaffected by arsenical treatment. *D. J. Bauer*

YAWS

Dillon, M. L. & Cooper, G. R. **Electrophoretic Analysis of Serum from Patients with Pinta and Yaws.** *Amer. J. Syph.* 1948, May, v. 32, No. 3, 251–5, 1 fig. [18 refs.]

" The electrophoretic analyses of three pinta and three yaws sera revealed a slightly increased content of γ globulin in the pinta sera and a larger increase in the γ globulin fraction of the yaws sera. The albumin content was proportionately low in comparison with the γ globulin content. No specific changes in the electrophoretic patterns indicative of the presence of unique proteins appeared in the diagrams of the pinta and yaws sera."

Vanbreuseghem, R. **Pianides psoriasiformes.** *Acta Tropica.* Basle. 1947, v. 4, No. 4, 353–4, 2 figs.

Report of a case in an African girl of 10.

LEPROSY

MUIR, E.; KIRWAN, E. W. O'G.; ADAMS, A. R. D. **Symposium on Leprosy. Recent Advances in the Treatment of Leprosy** [MUIR]. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Mar., v. 41, No. 5, 575–82. **The Eye in Leprosy** [KIRWAN]. *Ibid.* 583–90, 2 coloured figs. on pl. [16 refs.] **Three Cases of Leprosy treated with Diasone** [ADAMS]. *Ibid.* 591–4. Discussion 595–9 [MANSON-BAHR, P.; MAC ARTHUR, W.; COOKE, W. E.; BROWNLEE G.; CHESTERMAN, C. C.; GRAY, W. H.; MUIR, E.; KIRWAN, E. W. O'G.; ADAMS, A. R. D.]

The opener of this discussion dealt almost entirely with trials of the new sulphone drugs, promin, diasone, promizole and sulphetrone of Burroughs Wellcome & Co. on the lines of his earlier papers on the first two: arrest of the disease may be expected in the majority of lepromatous cases in about five years. Promizole was found less effective by U.S.A. workers and has been given up by them, as it is difficult to make, expensive and it presents no advantages except that it is slightly less toxic than some. Of greater interest is the statement that early reports on the use of sulphetrone indicate that it is less toxic and gives quicker results than the other sulphones yet tried. All of them require hospital treatment to enable resulting anaemia to be detected and treated with iron and liver preparations, to which Muir advises the addition of vitamin B in the form of yeast. In patients subject to reactions, small doses should first be given, such as 0·3 gm. of diasone or 0·5 gm. of sulphetrone, both orally every other day, cautiously increased to 2 gm. on alternate days. This point may be reached in a few weeks or it may take many months. In early uncomplicated cases the dosage may be increased more rapidly. A fall of haemoglobin below 70 per cent. is an indication to stop the drug, as is the occurrence of reactions. Destructive effects of sulphones on lepra bacilli are only well marked in the neighbourhood of capillary blood vessels. DAVEY has recently reported from Nigeria some lepromatous cases in which the lepromin test has changed from negative to positive within 5 to 10 months under sulphetrone. Tuberculoid cases, with few lepra bacilli, do not apparently respond as well to sulphones. Improvement occurs in most lepromatous cases in 2 or 3 years. Greatly increased accommodation and medical staff in resident institutions will be necessary to enable the prolonged sulphone treatment to be carried out in all lepromatous cases, but with the promise in time of greatly reduced numbers of highly infective cases.

KIRWAN spoke on eye infections in leprosy from a large experience in Madras, and gave a table of their frequency varying from 42 to 100 per cent. They occur in neural cases as a result of the exposure of the cornea owing to muscular paralysis, and in lepromatous cases owing to infection through the blood stream. The original paper should be consulted for detailed description. Treatment is difficult, but penicillin is advised locally for conjunctivitis. The slit lamp with the corneal microscope and the electric ophthalmoscope are essential for diagnosis.

ADAMS reported three lepromatous cases treated with diasone with marked retrogression of the skin lesions, but no obvious diminution of the bacilli. MACARTHUR spoke on misconceptions regarding the incidence of leprosy during Biblical and mediaeval times due to too literal interpretations of words which in early times had a wider and more general application than they now have.

BROWNLEE spoke on the toxic effects of sulphones and described the resulting anaemia as hypochromic at first, but later of the nutritional type. The latter

he attributes to a change in the intestinal flora which cuts down the biosynthesis of vitamins of the B-complex group : yeast treatment is indicated in such cases.
L. Rogers

AYCOCK, W. L. **A Proposed Study of Conjugal Leprosy with reference to Contagion and Hereditary Susceptibility.** *Internat. J. Leprosy.* 1948, Jan.–Mar, v. 16, No. 1, 1–8, 2 charts.

This paper discusses the possible light thrown by the incidence of conjugal infections on the difficult question of the relative influences of contagion and hereditary susceptibility. The following are the main points in a largely theoretical discussion. The occurrence of several cases in one family may be due to either contagion or heredity. The infection of twice as many males as females is more in keeping with the Mendelian operation of hereditary susceptibility. Data on conjugal leprosy might help to decide between susceptibility and prolonged exposure to contagion, but age susceptibility complicates the question. The rarity of conjugal leprosy allows of comparative studies of regional, racial and familial factors. More frequent child infections may be due to greater exposure to infection. Consideration of both the interval after conjugal exposure and the age at which the disease occurs would make it possible to distinguish between prolonged exposure and familial susceptibility as the probable determinant in conjugal infection. Reference is made to a previous paper by the author and GORDON [this *Bulletin*, 1948, v. 45, 186] on leprosy in veterans of American wars, which showed that Spanish American War veterans from non-leprous regions acquired their initial exposure on military service ; in World Wars I and II, veterans from foci of the disease were found to be infected during or shortly after their military service and developed their disease within a few years of beginning their service ; whereas Spanish War veterans developed theirs on an average of 23 years after their military service and at an age 20 years later than the former. It is therefore anticipated that conjugal cases may show a similar pattern of two groups of development of the disease, either soon after marriage or at a much longer interval, and at later ages. The latter are likely to have contracted the disease from their spouses ; the former through previous exposure in their own families. Further studies of conjugal cases on these lines are indicated. A suggested table for notes on cases of conjugal leprosy is given.
L. Rogers

SEN, P. **A Plea for the Study of Social Aspects of Leprosy.** *Leprosy in India.* 1947, Oct., v. 19, No. 4, 123–7.

DE SOUZA-ARAUJO, H. C. Descoberta e isolamento dum bacilo ácido-alcool resistente de carrapato ("Amblyomma rotundatum") capturado em sapo ("Bufo marinus"). "Mycobacterium lutzi", n. sp. Nota previa. [**Isolation of an Acid-Fast Bacillus from a Tick (*Amblyomma rotundatum*) captured on a Toad (*Bufo marinus*). "*Mycobacterium lutzi*", n. sp.**] *Brasil-Medico.* 1948, Jan. 17, 24 & 31, v. 62, Nos. 3, 4 & 5, 17–18, 2 figs. English version 18–19.

DE SOUZA LIMA, L. & DE SOUZA CAMPOS, N. **Immuno-Biologic Anomalies in Leprosy.** *Internat. J. Leprosy.* 1948, Jan.–Mar., v. 16, No. 1, 9–22.

In this important paper Mitsuda, or lepromin, reactions on 901 patients in 1941 are tabulated under the types of "uncharacteristic" and tuberculoid ; and the subsequent variations in the reactions and the evolution of the cases are examined. The sixteen tables should be studied in the original, but the following are the conclusions arrived at. Of 216 uncharacteristic cases 60 were

negative in 1941, 41, or 68·3 per cent., of which had developed into the lepromatous type by 1946. Of 139 positive cases, 33 or 23·7 per cent., became lepromatous. A much smaller proportion of strongly positive (3 plus) became lepromatous than of weak (1 plus) cases. Nevertheless, the general assumption regarding the prognostic value of the test is by no means universal. Among 685 tuberculoid cases 592, or 86·4 per cent., gave positive reactions, 79, or 11·5 per cent., negative and 14, or 2 per cent., doubtful reactions. Only 17, or 2·9 per cent., of the positive cases developed into the lepromatous type; but of the negative cases 29, or 36·7 per cent. became lepromatous, together with 1 of the 2 doubtfully reacting ones. The prognostic indications of the test were thus more accurate in the tuberculoid cases, but not absolute. In some cases of both types a change occurred from a positive to a negative type and *vice versa*. In 3 of the latter, the lepromatous type nevertheless developed; among those changing from positive to negative, lepromatous transformation occurred in all except one patient. *L. Rogers*

Box, Louise A. **Benadryl in Acute Lepra Reactions.** *Hawaii Med. J.* 1948, Mar.–Apr., v. 7, No. 4, 303–4.

The author reports on a trial of an anti-histamine drug, Benadryl (B-dimethylaminoethyl benzhydryl ether hydrochloride) in the allergic reactions of leprosy. The 9 treated cases include 3 with acute lepra reactions of spontaneous occurrence, 4 with acute lepra reactions apparently precipitated by promin treatment, and two with "major tuberculoid" reactions. The effects were compared with histories of previous reactions, of which it was not always possible to get reliable accounts. An average dose of 50 mgm. is given three times a day and continued from a few days to several weeks in accordance with the length of the reaction. The three spontaneous acute reactions appeared to respond well, as did the four which had followed promin treatment, but the two major tuberculoid ones gave equivocal results. The patients had no pain and no new lesions developed during a reaction. The author is cautious in coming to conclusions, but thinks further investigation of anti-allergic drugs in the treatment of acute leprous reactions is indicated. *L. Rogers*

Chandy, P. J. **Iodised Hydnocarpus Oil in the Treatment of Leprosy.** *Leprosy in India.* 1947, July, v. 19, No. 3, 72–9.

The author reports on the treatment of 44 cases, most of which were lepromatous and bacteriologically positive, by iodized hydnocarpus oil prepared by the following method so as not to contain any free iodine: 36 grains of resublimed iodine are dissolved in 1 ounce of ethyl ester of hydnocarpus oil; this iodine ester is then poured into a one pound bottle containing 15 ounces of hydnocarpus oil, the contents are well shaken and the whole is then sterilized in an autoclave at 15 lb. pressure for half an hour. Heat-proof glass bottles should be used. Injections are free from pain and as much as 10 cc. can be injected intramuscularly at one site without induration or other trouble and without serious reactions. The injections were given once a week for two years, to a total amount of over 400 cc. Nodules flattened and in time disappeared, bacilli decreased and the majority of the cases became bacteriologically negative, especially those in which the organisms were not very numerous at first. The results were better than with Hydnocreol. A table shows details of the cases. *L. Rogers*

DHARMENDRA & SEN, N. **Erythrocyte Sedimentation Test not necessary for regulating Treatment with Hydnocarpus Remedies.** *Leprosy in India.* 1947, Oct., v. 19, No. 4, 128–30, 6 charts on 1 folding pl.

" For regulating the dose of the hydnocarpus oil it is not necessary to take into consideration the results of the sedimentation index. The treatment can very well be regulated by the clinical condition of the patient. The sedimentation index does not provide any additional information."

DE SOUZA LIMA, L. Tratamiento experimental de la lepra. [**The Treatment of Leprosy.**] *Medicina.* Mexico. 1948, Mar. 25, v. 28, No. 552, 129–33.

The reason for calling this treatment experimental is not quite clear. The author states that chaulmoogra has a false reputation and that he has no belief in its efficacy for three reasons: 1. That good report of its use has been (in the Padre Bento Sanatorium) in tuberculoid forms, yet in about 98 per cent. of 200 cases this disease retrogressed spontaneously and the remainder progressed even to mutilation in spite of the treatment. 2. That observation over 4 years of " two lots " [the numbers of patients are not given] of non-characteristic forms of leprosy, one group receiving chaulmoogra, the other not, showed that the " same percentages were transformed into lepromatous, or tuberculoid, or retrogressed " in each group, so that the painful treatment with chaulmoogra had no effect and might just as well have been omitted. 3. That chaulmoogra did not influence the progress in a thousand cases under observation; those of the lepromatous form which seemed for a time to improve relapsed again within a comparatively short period. Chaulmoogra preparations were given intramuscularly or intradermally, in varied doses.

The author then relates his experiences with Promin, given intravenously each day, starting with 1 cc. and increasing gradually to 5 cc., administration being for a fortnight, followed by a week's remission. Next, with Diasone, given orally, in doses of 0·33 cgm. [0·33 gm. ?] daily for 6 weeks, followed by a rest for a fortnight. From these, singly or combined, excellent results are recorded, even in cases of ocular leprosy. In ordinary cases infiltration was reduced, discoloration gave place to a normal skin, and biopsy search for bacilli showed steady reduction. At first Diasone seemed to aggravate the skin conditions, infiltrations became more swollen, lesions extended and fresh ones appeared, but they soon cleared up if the treatment was persisted with.

H. Harold Scott

DAVISON, A. R. **Antimony in the Treatment of Leprosy.** *Internat. J. Leprosy.* 1948, Jan.–Mar., v. 16, No. 1, 23–8, 15 figs. on 2 pls.

Experience at the Pretoria Leper Iustitution supports the view that antimony has the power of controlling lepra reactions and benefits erythema nodosum leproticum. Insulin is also being used, but the author has not yet decided which is the better treatment. The drug is also of value in tuberculoid cases in the re-active phase and in neural cases which are developing new macules through having a lowered resistance. Fouadin is given in courses of ten intramuscular injections followed by a fortnight without treatment. Continued and intensive courses of antimony treatment were not beneficial. If antimony fails to build up resistance bismuth may be of value. The appearance of new lesions is an indication for stopping chaulmoogra treatment. Most of the cases were of the neural type, but in three lepromatous cases antimony helped to render them free from bacilli. Antimony may also be of

use as an adjuvant to promin treatment. Antimony is not a specific cure for leprosy, as failures have equalled the successes, and the treatment must be adjusted to every individual. *L. Rogers*

GASS, H. H. **The Use of Massage in Leprosy.** *Leprosy in India.* 1947, July, v. 19, No. 3, 80.

AUSTIN, C. J. **Central Leper Hospital, Makogai (Annual Report 1946).** *Fiji, Legislative Council. Council Paper No. 1.* 1948, Appendix 7, 20–27, 1 diagram.

MASIH, M. **Leprosy and Anti-Leprosy Work in Almora.** *Leprosy in India.* 1947, July, v. 19, No. 3, 81–5, 2 maps.

HELMINTHIASIS

DE MEILLON, B. **Aspects of the Natural History of Bilharzia in South Africa.** *South African Med. J.* 1948, Apr. 10, v. 22, No. 7, 253–60, 1 map. [16 refs.]

An account of this paper, which was read at a medical congress at East London, has been reviewed in this *Bulletin*, 1948, v. 45, 190.

See also p. 671, HEISCH, **A Parasitological Survey of Taveta.**

ERFAN, M. & TALAAT, S. **Demonstration of Schistosoma Ova in the Liver by Biopsy.** *J. Roy. Egyptian Med. Ass.* 1947, Dec., v. 30, No. 12, 663–4.

The authors obtained liver biopsies in 41 cases of Egyptian splenomegaly. The biopsy was carried out under local anaesthesia by means of a small-calibre lumbar puncture needle, the tip of which is " debevelled to act as a trocar and cannula." The instrument is pushed 2 to 3 cm. into the liver during full expiration, the trocar is withdrawn and a 10 cc. Record syringe fitted tightly to the cannula. Suction is applied, the cannula is pushed in another 2 to 4 cmm. and withdrawn while suction is maintained. The puncture is sealed with collodion. The preliminary anaesthesia is obtained by infiltration of the skin, the pleura and peritoneal covering of the liver with a total of 10 cc. of 2 per cent. novocain solution.

The liver substance obtained is washed in saline and digested in a centrifuge tube with 5 drops of 4 per cent. sodium hydroxide ; the tube is warmed until digestion is complete, when the material is centrifuged and examined for ova.

Schistosome ova were found in 21 cases : 11 were *S. mansoni*, 5 were *S. haematobium* and in 5 cases, ova of both species were found. In 4 cases, *S. haematobium* ova only were found in both liver and faeces specimens. In 7 of the 21 cases, faecal examinations were negative, but ova were found in the liver.

Ova were present in liver, faeces or urine in 39 of the 41 cases, which the authors state " practically disposes of the theory that hepatic bilharziasis is due to infection with male schistosomes".

In 19 of the positive cases having ova in the stools, the liver and spleen were enlarged.

In one case, ova were present in the liver although neither it nor the spleen was enlarged.

It is concluded that liver biopsy is a simple, safe and useful means of diagnosing hepatic schistosomiasis. *H. J. O'D. Burke-Gaffney*

LOVERIDGE, F. G., ROSS, W. F. & BLAIR, D. M. **Schistosomiasis : the Effect of the Disease on Educational Attainment.** *South African Med. J.* 1948, Apr. 10, v. 22, No. 7, 260–63.

KIESER [this *Bulletin*, 1948, v. 45, 526] observed the deleterious effect of urinary schistosomiasis on the scholastic attainment of children in Transvaal schools. In Southern Rhodesia, school-teachers in European Schools frequently suspect schistosomiasis as an explanation of forgetfulness and lack of concentration in some of their pupils, and it is striking how often this tentative diagnosis is confirmed by medical examination and parasitological investigation.

In the case of European children, tests were made in two boys' schools which were generally comparable except that one gave an academic and the other a modern education. In general, the average intellectual standard was higher in the former.

" Presumptive " infections were diagnosed by a cercarial antigen skin test and " proved " infections were those afterwards confirmed by the finding of ova in the urine or stools or both.

A table indicates that in both " presumptive " and " proved " infections the schistosomiasis rate was significantly higher in the boys from the modern school, the findings being 74 and 27 respectively from 91 boys, compared with 37 and 9 from 108 boys in the academic school. The statistical significance of these figures is shown.

In the case of African schoolchildren, an investigation was carried out on 365 pupils of both sexes in one school : those in 11 classes were grouped on school examination results into upper and lower halves in each class : a note was made of those who failed in the examination. The results are shown in a table, from which it emerges that the " proved " infection rate averaged 50 per cent. Nevertheless, these did not represent the main constituent of the lower half of each class ; indeed the infected children made a slightly better showing in " presumptive " and " proved " infections alike. For example, only 30 per cent. of the pupils were regarded as being uninfected on the " presumptive " criterion yet more than half of them were in the lower halves of the classes. Again, only 44 of 92 pupils who failed in their examinations had schistosomiasis. On the other hand pupils with proved infections took 25 out of the 44 places comprised by the first four places in each of the 11 classes. An additional 9 members of this group gave presumptive evidence of infection, so that some evidence of schistosomiasis was present in 77 per cent. of the pupils who won all the top four places.

It appears that schistosomiasis had no adverse effect on the educational attainment of these African schoolchildren and, indeed, the infected children seemed to fare better than the uninfected.

While admitting that the reason for this difference between the European and African children is not clear, the authors observe that the African child is exposed to schistosomiasis earlier in life than the European and that the disease is more chronic in him at school age. It also may be that one more helminth infection, added to an organism already perhaps overburdened with other parasitic or nutritional influences, may make little difference to the general lowering of the level of scholastic attainment : but this does not explain the better performance actually observed in the infected children.

H. J. O'D. Burke-Gaffney

FAUST, E. C. **An Inquiry into the Ectopic Lesions in Schistosomiasis.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 175–99, 1 fig. [64 refs.]

Ectopic schistosomal lesions have been reported with increasing frequency during recent years. Many among the American and Australian troops

engaged in the highly endemic schistosomiasis areas in the Philippine Islands acquired schistosomiasis, and among these ectopic lesions have been not uncommon. The subject is therefore one of current as well as of practical importance. In this paper the literature on the subject is reviewed in some detail, and the mode of origin of the ectopic lesions is critically examined. The author gives the following summary and conclusions, but the original should be consulted by those interested.

"1. Ectopic lesions in schistosomiasis are defined as those produced by immature or mature stages of schistosomes outside the portal-caval venous blood channels with their extension into the pulmonary arterioles. The lesions occasioned by the migration of young worms have been studied critically in experimental hosts but are not histologically described for man.

"2. Interpretation of the lesions produced by schistosomes in man or other definitive hosts requires background information on the usual route of migration of the larvae from the site of their entry into the body to their arrival in the intrahepatic portal vessel, the growth of the worms in this location, their subsequent passage against the venous blood current to the mesenteric venous radicles or vesical plexus where they mature and oviposition takes place, and finally the local and systemic tissue reactions to the presence of the worms in the body.

"3. Tabulation of published and other case histories of ectopic schistosomiasis, based on autopsy, biopsy, surgical intervention and substantial clinical data indicates that there are not less than 82 known cases with 86 separate sites where these lesions have been located. Twenty-one cases with 23 lesion sites are attributed to *Schistosoma haematobium*; 12 cases with 12 lesion sites, to *S. mansoni*, and 49 cases with 51 lesion sites, to *S. japonicum*. A majority of reported ectopic lesions in *S. haematobium* infection have occurred outside the brain and its blood vessels; a significant preponderance of those in *S. japonicum* infection have been in the brain, while those in *S. mansoni* infection are too few to show any significant anatomical predilection.

"4. The tissue reaction to schistosome eggs which escape from blood vessels into perivascular tissues is an acute inflammatory one in which histiocytes, epithelioid cells, giant cells, eosinophils, plasma cells and fibrocytes attempt to wall off the invading foreign body, with the eventual production of a pseudo-tubercle around each egg as a center. Nest [*sic*] of eggs were typically found within relatively circumscribed areas, so that each lesion consists of an aggregate of pseudo-tubercles forming a granuloma that varies in size from a pinhead to an orange. The smallest ectopic lesions have been found in the conjunctivae, the largest ones have occurred in the brain.

"5. From the time of entry of the metacercariae of the human schistosomes into the cutaneous venules, following exposure to infection, the worms are characteristically intravascular in their location. There are several records of ectopic location of the adult worms, one in the middle cerebral vein, one in the ophthalmic vein, one in a coronary artery, and larger numbers from gastric, splenic esophageal, hepatic and renal veins of heavily infected experimental animals. In no instance is there any evidence of local tissue reaction to the presence of the worms.

"6. Five separate theories have been adduced to account for ectopic lesions in schistosomiasis: (1) Metacercariae develop to adult worms, with subsequent oviposition, at or near the sites of penetration into the skin or mucous membrane; (2) a patent foramen ovale would provide a direct route from the inferior caval veins into the systemic circulation; (3) eggs may escape through the pulmonary capillaries and be deposited in distant arterioles; (4) adult worms may travel against venous blood flow into collateral vessels and on reaching the end venules deposit their eggs, and (5) the vertebral

venous system provides a natural, valveless intercommunicating channel from portal and caval veins to all parts of the body, without need of embolic filtration of eggs or the migration of adult worms against blood flow or valves.

The first theory is contrary to all critical studies on the development of schistosomes in the body of the definitive host. The second theory predicates a highly improbable combination of circumstances but might possibly explain the presence of a male worm discovered in a branch of the coronary artery. The third theory is discounted by the characteristic disposition of eggs in nests or aggregates, and tissue reaction around venules rather than arterioles. The fourth theory provides a rational explanation in case the worms migrate against venous blood flow into valveless veins. The fifth theory provides an adequate basis for all but one of the ectopic lesions which have been described.

"7. Ectopic lesions in schistosomiasis are not rare, although the cases described are few compared with the millions of cases of intestinal and vesical schistosomiasis. It is significant that during the period 1942–1947 more ectopic cases were reported than from 1889 through 1941, and that autopsy diagnosis has declined while diagnosis by biopsy and surgical removal of the lesion has increased.

"8. Ectopic lesions in schistosomiasis, particularly those involving the central nervous system, may be anticipated even several years after intestinal or vesical symptoms have disappeared; moreover, these lesions may develop without a previous clinical history or diagnosis of the disease.

"9. Chemotherapy is essential for all cases of schistosomiasis diagnosed by ectopic lesions, to prevent additional ectopic complications, even though there may have been no history or diagnosis of abdominal schistosomiasis. The present drug of choice is potassium antimony tartrate, administered intravenously in a one-half per cent. solution on alternate days for approximately four weeks." *A. R. D. Adams*

AFIFI, M. A. **Bilharzial Cancer. Radiological Diagnosis and Treatment.** Foreword by Sir Alfred WEBB-JOHNSON. pp. viii+111, 60 figs. 1948. London: H. K. Lewis & Co., Ltd. [16*s*.]

This excellent little book consists of three parts, namely, I. Relationship between Bilharziasis and Cancer; II. Radiological Diagnosis of Bilharzial Cancer; and III. Treatment of Bilharzially Associated Cancer. Dr. Afifi is careful to point out that the term "Bilharzial Cancer" is somewhat misleading, for there is little or no evidence that *Schistosoma* is a specific cause of cancer, though the chronic inflammation which it causes may, in common with other inflammatory agents, play a subsidiary rôle in localizing the disease. When one recalls that in some parts of Egypt, over 90 per cent. of the population are infected with *Schistosoma* it is not surprising that this organism is frequently present in association with malignant disease, especially in the bladder, which is the commonest site of infection with this organism; and though vesical cancer at once comes to mind from the title of the book, almost every organ of the body, whether the seat of cancer or not, may be subject to *Schistosoma* infection. Concerning diagnosis, plain radiography reveals the infection of the bladder if enough calcified ova are present in the tissues to cast a shadow. Further information is gained by the use of contrast media, such as sodium iodide, introduced into the bladder by catheter before the photography. In this way, a distorted vesical outline or a filling defect can often be revealed. In early stages of the disease cystoscopy is, of course, a help, but a large proportion of the cases when first seen by Dr. Afifi were already too advanced for this kind of investigation. Pneumocystography may be of help in some instances. The X-ray diagnosis of schistosomiasis of the bladder and other organs is well illustrated by numerous radiographs.

The treatment of cancer in any organ is the same whether schistosomiasis is present or not, except that if living ova are present it will be necessary to give the patient a course of tartar emetic or other parasiticide. Surgery has been ineffectual, death within a year having been an almost constant sequel; most of the cases were already far advanced before the patient came to hospital. Deep X-ray therapy has given some alleviation and perhaps an extension of life. The usual method has been the use of 200 kv., 2 mm. Cu, at 50 cm. distance with 150 cm. fields. The percentage depth dose with this is about 37. Four of these fields are used, three being applied to the abdomen—mesially and on each side—and one to the perineum, with centres directed on to the growth on each occasion. Contact radio-therapy is in the experimental stage and its value has not yet been determined.

This book is informative, concise and easy to read, and will be of value to everyone interested in *Schistosoma* infection or in cancer of the bladder.

Harold Burrows

TALAAT, S. M. & SHOAIB, S. **The Intensive Treatment of Bilharziasis with Tartar Emetic.** *J. Roy. Egyptian Med. Ass.* 1947, Dec., v. 30, No. 12, 598–607, 5 charts.

The authors, searching for "a more suitable treatment than the one at present in general use", tried several types of intensive treatment.

They were unable to give the course of treatment described by ALVES and BLAIR [this *Bulletin*, 1946, v. 43, 344] as in the five cases tried they were compelled to cut short the course at the third or fourth injection because of circulatory collapse.

Giving 32 patients one intravenous injection of 2 grains of tartar emetic daily for twelve days, they believed 30 to be cured.

Another set of 25 patients was treated by giving two injections daily, the injections being given six hours apart, for five days, a total of 20 grains of tartar emetic. One patient dropped dead two days after completion of the course. None of the other patients failed to respond to the treatment in which, however, toxic effects were well marked. This course is not recommended by the authors.

A six-day course of one injection daily [2 grains tartar emetic] was a complete failure.

The authors next describe a three-day ambulatory course in which two injections were given daily at six-hourly intervals. Of the 22 patients treated, two could not be followed up, while 20 became "ova free." There were some toxic effects; in most cases, they were not serious.

Only 13 out of 20 patients ceased to pass eggs when treated with a one-day course of three injections, three hours apart.

The course finally recommended by the authors is a two-day regimen in which two injections at six-hourly intervals are given on two consecutive days (8 grains tartar emetic). The toxic effects with this course are "no graver than those seen with the standard method of therapy" and eighteen out of 20 patients passed their criterion of cure, which was the repeated absence of living ova after a follow-up of one month. Two of the patients were splenectomized after the course and were negative 2½ months later. [Work of this kind on the antimony therapy of bilharzia is exceedingly useful, while such drugs as "Miracil" remain unevaluated, but it is a great pity that workers do not make their methods and results perfectly clear. The authors state that they treated patients of from 9 to 50 years with "tartar emetic" but nowhere state whether the sodium or potassium salt was used. They used an adult dose of 2 grains per injection, but do not state what percentage of their cases were children, nor what dose they administered to such patients.

One patient with a haemoglobin of 35 per cent. died and the reader is left to assume that one of their criteria of fitness for treatment, *i.e.*, a minimum haemoglobin level of 50 per cent., was instituted after this mishap.

In successive paragraphs, they say (1) " It is also known that the drug is excreted in 2–3 days through the kidneys . . . " and (2) " With the standard methods of treatment . . . the drug remains in the body for a month on an average."

Five charts are given, intended to show the number of days taken to produce ova-free urine, but it is impossible to correlate the numbers given in the text with those given in some of the charts. Nevertheless, their two-day course is worthy of extended trial and should be very valuable in hospital work.]

W. Alves

SAID EL AYADI, M. **Treatment of Bilharzia by the Oral Route.** *J. Roy. Egyptian Med. Ass.* 1947, Nov., v. 30, No. 11, 562–6.

Ten million of the population in Egypt suffer from chronic schistosomiasis. Parenterally administered trivalent antimony is unsuitable for mass treatment of the population for this infection. Methods of treatment with antimony by the oral route were investigated, attention being directed particularly to the avoidance of emesis, to the promotion of absorption of the drug from the intestine, and to the establishment of the effective dosage of the selected compound.

Repodral (Fouadin) in 6·3 per cent. solution was selected for trial. Tolerance to its administration by the oral route was found to be increased by giving the drug in small amounts at intervals of 2½ to 3 hours on an empty stomach. Beginning with 4·5 ml., divided into 5 doses, during the first day, the amount was increased daily until on the 6th day 8·2 ml. were given ; the gross dosage in this period was 40·0 ml. There was no vomiting as a result of the treatment. [The number and the weight of the persons used in this experiment are not stated.]

Of the substances [unspecified] examined to promote absorption of antimony from the gut, riboflavin in doses of 2·5 to 3 mgm. was found " to produce the desired effect." Its action is likened to that of vitamin D on calcium, and vitamin C on iron, absorption.

Dogs were injected with a total of 0·4 ml. of Repodral per kgm. of body weight as described by HALAWANI and ABDALLAH [this *Bulletin*, 1947, v. 44, 220]. On examination 24 hours after the last injection, the antimony content of the liver was found to be about 3·5 mgm. per cent. This amount of antimony is [assumed by the authors to be] that in human livers found by the above-mentioned workers to be lethal to schistosomes in 12 of their 15 patients. The oral dosage necessary to produce this level of antimony in the livers of dogs was 2 ml. per kgm. body weight.

Four *Cercopithecus griseo-irridis* [*sic.* ? *griseoviridis*] were infected with *Schistosoma haematobium* ; eggs appeared in their stools after 84 days. Two of the monkeys were treated with riboflavin and Repodral (2 ml. per kgm. divided into 6 doses over three successive days). A third monkey was treated with 0·6 ml. per kgm. for two doses only. The fourth was untreated.

The number of ova in the stools of the three treated monkeys gradually decreased over a period of a month ; the proportion of dead ova steadily increased, until after 10 to 15 days no living and only an occasional dead ovum was found. After 25 days, no more ova were found in the two fully treated monkeys ; there were scanty living ova from the incompletely treated monkey ; the control still produced living ova. The incompletely treated monkey was then given 0·34 ml. per kgm. of Repodral ; no ova were subsequently

ound over one week's daily observation. It is concluded that oral treatment of schistosomiasis with 2 ml. Repodral per kgm. of body weight, with riboflavin, is curative ; 0·66 ml. per kgm. is not curative ; 1 ml. per kgm. may be so.

A. R. D. Adams

HALAWANI, A., NEWSOME, J. & WOOTTON, I. D. P. **Miracil D : Investigation of Blood Levels after a Single Dose.** *J. Roy. Egyptian Med. Ass.* 1947, Dec., v. 30, No. 12, 656–62, 2 figs. (1 folding).

Miracil D or Nilodin is a new remedy recommended for the treatment of schistosomiasis [this *Bulletin*, 1948, v. 45, 526]. In this study, 400 mgm. were given as a single oral dose to each of 22 male Egyptian patients. The blood concentration was measured by the method of LATNER, COXON and KING [this *Bulletin*, 1948, v. 45, 96] with slight adaptations. In patients with normal kidney function, the blood level rose to a maximum at 12 hours and fell almost to zero by 24 hours. The maximum ranged from 60 mgm. to 400 mgm. per 100 ml. In patients with a renal clearance of less than 50 per cent., the 12-hour blood concentration ranged from 140 to 350 mgm. per 100 ml. and the concentration was often still high at 24 hours. Impaired kidney function causes the blood level to be higher and more sustained than it is in normal persons. In order to maintain a persistent high level in the blood, it is recommended that miracil should be given at intervals of 12 hours ; with patients who have poor kidney function, it may be enough to give it every 24 hours. *F. Hawking*

GELFAND, M. **Cysticercosis of the Brain in the African of Rhodesia.** *East African Med. J.* 1948, Mar., v. 25, No. 3, 110–12.

Between 1940 and 1945, the author found seven cases of cerebral cysticercosis in 2,148 autopsies in Salisbury Native Hospital, Southern Rhodesia. There were also three cases of cysticercosis of the heart, one of which also showed the cerebral form. The cysts were commonly seen in varying numbers over the frontal and parietal lobes and occasionally in the occipital region : in two cases, they occurred on the cerebellar surface. The cysts were always found on the brain surface, but never in its substance.

The Mashonaland African eats locally bred pig, but infected pork is liable to be eaten by him through ignorance, since the same system of meat inspection which exists in more advanced communities is not available to the local African who is therefore more liable to cysticercosis infection than is the European. The author has not seen a case in a white resident of Rhodesia.

The principal clinical feature of cerebral cysticercosis is recurrent epilepsy, with a varying number of seizures : the disease may often terminate in *status epilepticus*. Other mental conditions are described, but the author has not noted them in Africans.

Diagnosis is not easy, and depends on the demonstration of cysts which may not always be detectable by X-ray as calcification does not necessarily occur. Careful palpation may reveal the presence of cysts in the muscles, especially in the arms, shoulder regions and chest wall. They are about the size of a pea, oval or elongated and vary greatly in number.

In the brain, the cysts vary in size from a few millimetres to $\frac{1}{4}$in. to $\frac{3}{4}$in. There may be only one cyst or very many and this variability in size, number and distribution is very great. When the cyst dies, toxic substances are formed which cause necrosis in the surrounding tissues : later the necrotic tissue becomes fibrosed into a capsule having an inner layer of connective tissue and an outer cellular layer.

The author discusses the diagnosis and points out that eosinophilia is of little diagnostic value in tropical Africa. He has had no experience with the complement fixation test in this condition. X-ray of a suspected area is advised and the examination of an excised cyst will clinch the diagnosis. A lateral view of the skull usually suffices and the opacity found varies from 1 mm. in the case of a calcified scolex to the size of a fully grown cyst. The author has found nothing characteristic in the cerebrospinal fluid, although a pleocytosis has been described.

The other causes of epilepsy in the African are discussed. The author has usually observed that it begins in adult life. In many cases, no cause can be found and the possible part played by malaria and schistosomiasis is considered. No schistosome ova were found in brain tissue from 40 consecutive autopsies on those proved to have urinary and intestinal schistosomiasis.

H. J. O'D. Burke-Gaffney

LOUGHLIN, E. H. & STOLL, N. R. **Hookworm Infections in American Servicemen with reference to the Establishment of *Ancylostoma duodenale* in the Southern United States.** *J. Amer. Med. Ass.* 1948, Jan. 17, v. 136, No. 3, 157–61. [Refs. in footnotes.]

The authors review the recent literature on hookworm infection among returned American servicemen. Taking into account the fact that some men, especially those from the Southern States, left the United States for service in the Pacific with hookworm infections, and the proportion of the Pacific-acquired infections that were due to *Ancylostoma duodenale*, they arrived at the following figures :—*Ancylostoma* was present in 2 of 100 men of the garrison forces in Guam, in 7 of 100 men with Pacific duty, undifferentiated, and in 30 of 100 of the marines returned from Leyte. *A. duodenale* infections were also contracted in Assam and Burma.

The infections were usually, but not invariably, light. The average post-treatment counts in three groups of 10, 100 and 20 patients were respectively 88·6, 10 and 17 adult *A. duodenale.*

Various estimates have been made of the pre-service hookworm infection rates : the authors conclude that 18·1 per cent. may be taken as the infection rate (*Necator americanus*) for men recruited from the southern coastal States. This indicates the persistence of unhygienic conditions in these States.

The return of a considerable number of infected servicemen (1 in 15 of returned veterans) combined with the evidence of persistence of bad hygienic conditions indicates a danger that *A. duodenale* may become established in the Southern States.

The authors conclude by stating " confirmation of such suspicion must await discovery of the first instance of proved autochthonous infection".

L. E. Napier

WALLACE, F. G., MOONEY, R. D. & SANDERS, A. *Strongyloides fülleborni* **Infection in Man.** *Amer. J. Trop. Med.* 1948, Mar., v. 28, No. 2, 299–302, 2 figs. [11 refs.]

A U.S. veteran, who had had 3 years service in the South-West Pacific, including 4 months in Guadalcanal, 12 in Fiji, 12 in Bougainville, and 8 in Leyte, which terminated 19 months previously, was found to have ova of *Strongyloides* in his stools, on every examination over a period of 5 weeks.

In the laboratory, these hatched within 12 hours and developed into rhabditiform larvae, then into free-living male and female adults which produced a second generation of rhabditiform larvae from which infective larvae were

produced. The experiments did not exclude the possibility that there was some direct development from the original rhabditiform larvae into infective larvae.

The constant appearance of ova in the stools raised doubt as to the identity of the *Strongyloides* and it was eventually identified as *Strongyloides fülleborni* from the morphology of the female adult. SANDGROUND [this *Bulletin*, 1926, v. 23, 758] and GOODEY [*ibid*, 759] agree that among the clear-cut specific characters which identify *S. fülleborni* are prominent vulvar lips and narrowing of the body immediately behind the vulva in the free-living female. These characters were clearly identified in the specimens from the case. Further, the prominent oesophagus in the free-living stages supported the identity.

This species is found in monkeys of several genera. Monkeys (*Macaca* sp.) in the animal colony of the University of Minnesota were consistently infected with *S. fülleborni*. STILES and HASSAL (*Hygienic Lab. Bull.*, Washington, 1929, No. 152) list the Philippine Islands among the localities where the species is found.

The patient had kept a pet monkey while on Leyte. It appears that this was a specimen of *Macaca irus*, the only monkey native to the Philippine Islands.

No symptoms were attributable to the strongyloid infection, but the man had amoebic dysentery for which he received appropriate treatment and was apparently cured.

[No mention is made of treatment for the strongyloid infection.]

L. E. Napier

DUNCAN, N. A. **Pancreatitis due to Ascariasis.** [Correspondence.] *Brit. Med. J.* 1948, May 8, 905.

Report of a fatal case in a boy of 18 months.

LOVETT-CAMPBELL, A. C. **The Surgical Treatment of the Large Elephantoid Scrotum.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Mar., v. 41, No. 5, 645–6, 8 figs. on 4 pls.

The removal of the large elephantoid scrotum is often easier than is the case with tumours of small or moderate size. The downward traction exerted by the weight of a large tumour causes the loosely attached healthy lower abdominal skin and Camper's fascia to descend like an apron over pubis and penis. This thin, supple, vascular sheet of skin and fascia, whose lymph channels are unimpaired, can be used to provide an excellent anterior flap for refashioning the scrotum after all tumour tissue and scrotal skin below have been excised. The flap has an excellent blood supply from branches of the epigastric arteries, as well as from the deep circumflex iliac artery, and the horizontal incisions by which the flap is raised do not cut across the general direction of the cutaneous vessels. The cords and testicles are freed in the usual manner and the penis brought through a hole cut in the flap, which is then sutured to the perineal margins to cover the roughly triangular raw area with its apex at the perineal body, thus forming the new scrotum. Large hydroceles have to be dealt with before replacement within the newly fashioned scrotum, and the base of the preserved penile skin is sutured to the edges of the aperture made in the skin apron. Eight excellent figures make the details of the operation clear.

[This method of reconstruction of the scrotum is only applicable to *very large* tumours. In other cases there is insufficient healthy skin available for forming an anterior flap.] *W. L. Harnett*

PATEL, J. C. **Antimony and Filariasis (*W. bancrofti*). Progress since World War II.** *Indian J. Med. Sci.* 1948, Mar., v. 2, No. 3, 151–62. [25 refs.]

A general review.

DEJOU, L. Kystes suppurés et abcès chroniques par vers de Guinée. **[Suppurative Cysts and Chronic Abscesses caused by Guinea Worm.]** *Bull. Méd. de l'Afrique Occidentale Française.* 1947, v. 4, No. 2, 121–3.

PUBLIC HEALTH REP. Wash. 1948, Apr. 9, v. 63, No. 15, 478–88. [15 refs.] **Control of Trichinosis. Report by the Committee on Public Health Relations, the New York Academy of Medicine.**

See *Bulletin of Hygiene*, 1948, v. 23, 592.

DEFICIENCY DISEASES

WATERLOW, J. C. **Fatty Liver Disease in Infants in the British West Indies.** *Medical Research Council. Special Report Series No. 263.* 84 pp., 5 text figs. & 26 figs. on 12 pls. [214 refs.] 1948. London: H.M. Stationery Office. [2*s*.]

Among infants in the British West Indies a syndrome has been observed of which the main features are oedema, muscular wasting and fatty infiltration of the liver. The condition is clearly related to the disease reported from several parts of Africa and known as kwashiorkor or infantile pellagra, but differs from it in that such manifestations of vitamin B complex deficiency as buccal ulceration, fissuring of mucocutaneous junctions and depigmentation of skin and hair which are regarded as characteristic of kwashiorkor, are often absent and never severe in the West Indian cases. Fatty change in the liver is regarded as the fundamental lesion and appears in West Indian babies in a relatively pure form, whereas in Africa it appears as part of a multiple deficiency state in which the clinical picture is complicated by the presence of various avitaminoses.

In accordance with this view, evidence of liver damage was used as the criterion for selecting the 15 cases described in this report.

In the majority of cases the condition appeared soon after weaning, at which time the diet consisted mainly of carbohydrate and contained very little milk. That inadequacy of diet at this period of life is widespread in the West Indies is also shown by weight curves; the growth rate falls off markedly during the six months after weaning.

The presenting complaints were oedema and vomiting. There was gross muscular wasting, but subcutaneous fat was not completely lost; in consequence of this and of the presence of oedema, the degree of weight-loss was less than in many cases of simple starvation. The liver was enlarged, and hepatic failure appeared to be the primary cause of death in four of the five fatal cases.

Further investigation revealed a moderately severe anaemia which was hypochromic and either normocytic or slightly macrocytic in type. Serum protein concentration was low (less than 4·5 gm. per 100 ml. in 8 cases), the reduction being mainly in the albumin fraction. The serum phosphatase values were similar to those found in control cases of simple undernutrition; there was slight hyperbilirubinaemia. The only test of liver function which proved of value was the bromsulphthalein clearance test, and this showed impairment in all cases. The fat content of the stools was increased; the proportion of split fat was normal.

Post-mortem examination in four fatal cases showed gross fatty infiltration of the liver ; the fat in the liver was neutral fat ; the phospholipid content was low. The only other abnormal findings were atrophy of voluntary muscle fibres, atrophy of the acinar cells in the pancreas and a moderate and variable amount of iron pigmentation in the liver.

Fatty infiltration was also demonstrated in surviving cases by means of liver biopsy, and repetitions of this procedure, with serial measurements of serum protein and bromsulphthalein clearance, were used to assess the response to treatment.

Administration of methionine, choline and inositol, in the doses used, appeared to be without effect ; on the other hand, improvement occurred on a high intake of milk.

In addition to the 15 cases upon whom detailed investigations were carried out, 600 unselected babies of between six months and two years were examined clinically, and enlargement of the liver without oedema was found in over 10 per cent. of them. In two of these cases of symptomless hepatic enlargement, further investigation showed normal serum protein concentration and normal, or almost normal, bromsulphthalein clearance, but liver biopsy revealed the presence of fat. It is concluded that such cases of simple hepatic enlargement represent an early stage of fatty liver disease, and this figure gives some idea of the probable prevalence of this condition.

Cirrhosis of the liver is not uncommon in children in that part of the West Indies where fatty liver disease is commonest ; material obtained by biopsy and at post-mortem upon cases of fatty liver disease provides some evidence that cirrhosis develops as a result of preceding fatty infiltration, and represents the final stage of the disease in those affected who neither die nor recover completely.

As regards the aetiology of the condition, the dietary histories, the absence of evidence of any infection or intoxication and the exogenous source of the liver fat led to the conclusion that fatty liver disease is due to malnutrition. The rarity and inconstancy of associated manifestations of vitamin deficiency suggest that the condition is not due to a specific avitaminosis, and therapeutic tests have shown that it is not due to deficiency of such factors as choline and methionine, which are lipotropic because they act as sources of labile methyl groups. It is, however, clearly associated with a low protein intake and a relative overloading with carbohydrate. Yet the picture is entirely different from that of simple starvation in which the protein intake is often equally low, in that in the latter condition there is loss of all body fat and no fatty infiltration of the liver. The factor determining which of the two clinical and pathological conditions is produced in protein deficiency and protein depletion appears to be the level of caloric intake, deposition of exogenous fat in the liver only occurring when there is a *relatively* high caloric intake.

Waterlow's work is of importance beyond the mere collection of new clinical, biochemical and pathological data about an interesting deficiency state. Although the exact cause of fatty liver disease in infants remains unknown, all that this investigation contributes tends to suggest that the ultimate solution of the problem will be found in an imbalance of nutrient intake, a distortion of metabolic pattern, rather than in any single specific deficiency. Advance has been made in defining the unsolved problems and in showing which of the results of experiments upon nutritional liver damage in animals, here discussed in detail, are or are not applicable to human pathology.

[The finding by Waterlow of a pancreatic lesion is of particular interest. Similar lesions have recently been described by other authors (see below) and the theory has been put forward that pancreatic damage is the fundamental lesion in the syndrome.]

There can be no doubt that fatty liver disease is widespread in the tropics and is an important contributor to the appallingly high infant mortality rate of many tropical territories. Indeed, recent work suggests that the condition is not confined to the tropics (VEGHELYI, *Lancet*, 1948, Mar. 27, 497). There is here abundant evidence that a high carbohydrate, low protein diet given after weaning is an important, if not the only, causative factor. The feeding of pap made from a variety of cereals, with an inadequate intake of milk or other good source of protein, is an exceedingly widespread practice throughout the world and a clear indication is given of the effect that correction of this dietary fault might be expected to have on infant health. Further, evidence is produced that the development of cirrhosis of the liver in young people, also a common and fatal disease in the tropics, may, in some cases, be traced to fatty liver disease in infancy. [See also this *Bulletin*, 1947, v. 44, 841 ; 1948, v. 45, 635.] *Dean A. Smith*

HOLMES, E. G. & TROWELL, H. C. **Formation of Hepatic Glycogen in Normal Africans and in those suffering from Malignant Malnutrition.** *Lancet*. 1948, Mar. 13, 395–8, 2 figs.

The formation of hepatic glycogen was studied in human subjects by estimations on samples of liver obtained by biopsy. As the authors point out, although it has been shown in experiments on animals that liver glycogen increases after glucose is given, this has never yet been directly demonstrated in man. For this reason alone the results are of great interest.

The subjects fasted overnight. In the morning, an initial sample of blood was taken for blood-sugar and serum-protein estimations and the initial biopsy was made ; 50 gm. of glucose were then given intravenously, and blood samples were taken after one hour and two hours. Biopsies of the liver were made in earlier tests after two hours, in later tests at both one and two hours after glucose had been given. The tests were made on four control subjects, eight patients with malignant malnutrition, one recovered patient, and one with sub-acute hepatic necrosis. With one exception—a child of two years—all the patients with malignant malnutrition were adults. The clinical picture in these cases has already been described [this *Bulletin*, 1946, v. 43, 363].

In both controls and malnourished subjects, the initial levels of liver glycogen showed wide variation (from about 10 to about 40 mgm. per gm.) In all the controls, the glycogen increased after glucose was given : the increase was sometimes greater at one hour than at two hours. In the patients with malignant malnutrition, the liver glycogen either fell or remained unchanged. In the one case of subacute hepatic necrosis, the initial level was low but was more than doubled two hours after glucose was taken.

The blood sugar in the controls had fallen almost to the initial level two hours after the test dose of glucose. In the malnourished subjects, on the other hand, it remained high. There was therefore a diminished glucose tolerance. Oral glucose tolerance tests in cases of malignant malnutrition showed a similar delayed fall in blood sugar.

The conclusion is drawn that in the patients with malnutrition the liver was unable to synthesize glycogen from glucose at the normal rate. It must, however, have retained some power of forming glycogen from other sources, if not from glucose, since it was by no means glycogen-free. Moreover, the power to mobilize glycogen could not have been entirely lost, since, with one exception, hypoglycaemia was not found even after 24 hours' fasting. [It is of interest to compare these findings with those of BOSE [see *Bulletin of Hygiene*, 1947, v. 22, 406) who found impaired glucose tolerance and low resting blood-sugar values in both acute and chronic starvation.] [See also DAVIES, this *Bulletin*, 1948, v. 45, 633.] *J. C. Waterlow*

GILLMAN, J., GILBERT, Christine & GILLMAN, T. **The Bantu Salivary Glands in Chronic Malnutrition with a brief consideration of the Parenchyma-Interstitial Tissue Relationship.** *South African J. Med. Sci.* 1947, Sept., v. 12, No. 3, 99–109, 8 figs. on 2 pls. [27 refs.]

The Gillmans and their colleagues in Johannesburg, in their work over a number of years on the pathological histology of malnutrition in Africans, have not confined themselves to descriptive observations, although the facts so gained are of the first importance. They have in addition persistently tried to visualize the reactions of the body as a whole in a particular setting over a period of time—an approach that is both fruitful and stimulating.

The present paper is an example of this. The salivary glands have been little studied by morbid anatomists, because they are regarded as unimportant appendages. In fact, however, they can give useful information, for, as the authors point out, " the modifications in the structure of the salivary glands in human malnutrition represent only a facet of the more general alterations in metabolism, in which many other organs and tissues are implicated ".

It is impossible to summarize briefly the details of the histological findings ; for these, the original paper must be consulted. The main changes found in cases of malnutrition were :—

i. Atrophy of the glandular tissue. The acini were reduced in size, or had disappeared completely. Sometimes the cells reverted to a cubical shape, indistinguishable from that of the epithelium lining the small ducts. The serous cells were more susceptible to atrophic changes than the mucous cells.

ii. Cystic dilatation of the ducts.

iii. Patchy accumulation of lymphocytes, particularly near the excretory ducts.

iv. Low-grade fibrosis, mainly round the ducts.

v. Cytosiderosis, seldom as severe as in the liver.

When atrophy of acini, dilatation of ducts, and fibrosis occurred together, the end-result closely resembled the picture of cystic fibrosis in the pancreas.

In the parotid the changes were rather different. Enlargement of the parotid has frequently been noted in malnourished Africans. This seems to be caused mainly by an increase in size of the individual gland cells ; there may also be an interstitial accumulation of fat. Parotid changes of this kind were found almost exclusively in males. Mixed parotid tumour is commoner in Africans than in Europeans, but other neoplasms of the gland are rare.

In the submaxillary and sublingual glands, the range of reactivity was similar to that of the liver, since it included atrophy, fibrosis, and cytosiderosis. Fatty change, however, was less common than in the liver, and less severe. The fact that fibrosis could occur without being preceded or accompanied by fat supports the view previously expressed by GILLMAN and GILLMAN [this *Bulletin*, 1948, v. 45, 632] that there is no causal relation between fibrosis and fatty change. Similarly, atrophy and fibrosis occurred quite independently. It is therefore suggested that " an overgrowth of connective tissue, whether it occurs in the liver, pancreas, or salivary glands, does not pre-suppose any observable injury to the parenchyma, although such injury may indeed be manifest at the chemical level ". However, as in the liver, so in the salivary glands, one form of connective tissue overgrowth seems to be related to factors controlling the distribution of lymphocytes, since fibrosis is commonly associated with lymphocytic infiltration. It is suggested that there may be a general stimulation of the reticulo-endothelial system in response to large molecules, which are either produced endogenously, or absorbed from the gut as a result of defective pancreatic secretion. [For comment, see below.] *J. C. Waterlow*

MAGALHÃES CARVALHO, SCHMIDT, M. M. & PINTO, A. G. Síndrome celíaca pos-distrofia pluricarencial hidropigênica. [**Coeliac Syndrome following Multiple Nutritional Deficiency with Oedema.**] *J. Pediatria*. Rio de Janeiro. 1947, July, v. 13, No. 7, 141–51, 3 figs. & 2 graphs. [22 refs.]

In previous papers [this *Bulletin*, 1948, v. 45, 635] Dr. Magalhães Carvalho and his colleagues in Rio de Janeiro have described infants and children with oedema, fatty liver, and signs of multiple nutritional deficiency. The condition is considered to be identical with kwashiorkor in Africa. They have now observed that many cases convalescing from this disease develop, after 4–5 weeks, the clinical picture of the coeliac syndrome. The abdomen becomes protuberant, and the stools pale, bulky, and offensive. In spite of a voracious appetite the child remains thin, and may show residual signs of avitaminosis.

Twenty-four hour specimens of faeces were collected from three such children on a mixed diet, which provided about 24 gm. of fat a day. Three other cases were put for three days on a diet of bananas and butter, which was calculated to provide 50 gm. of fat daily. Faeces were collected on the third day. Analysis showed that in both groups the faecal fat content was within normal limits, and the proportion of unsplit fat was normal, except in one case. The faeces in these experiments were not collected quantitatively ; however, in other similar cases the total weight of faeces excreted each day was measured, and found to be many times greater than normal. It is therefore argued that steatorrhoea did in fact exist, although it is not apparent from the figures for faecal fat content. The fact that there was no increase in unsplit fat is attributed to the fat-splitting action of bacteria in the period between collection and drying of the faeces.

The functional capacity of the pancreas was investigated in six cases by measuring the enzyme content of juice aspirated from the duodenum. The child was given no food overnight, and a tube was passed into the duodenum ; 10 ml. of 33 per cent. magnesium sulphate were given through the tube to stimulate bile flow, and a sample of bile was collected. Ten ml. of warm milk were then given ; 20–40 minutes later a sample of juice was aspirated, and after a further period of 20–40 minutes a second sample. The trypsin and lipase contents of the samples were measured ; estimations of amylase were abandoned as unreliable. The measurements were made by standard methods, and are not described in detail. In all the cases, both the trypsin and the lipase content of the duodenal juice were below the lower limit of normal. For trypsin this limit is given as 10 units, while the range in the cases investigated was from 2 to 8 units. For lipase the range was from 2 to 30 units, compared with a normal lower limit of 50 units. No measurements were made on control cases.

In discussing their findings, the authors suggest that there may be a connexion between pancreatic damage and fatty liver. They leave open the question of whether there is a definite causal relationship between functional impairment of the pancreas and the clinical manifestations of the coeliac syndrome.

[Although it is necessary, as GILLMAN *et al.* point out, " to avoid the narrow perspectives often resulting from too great a concentration on one gland, such as the liver ", yet it is inevitable that in the study of any disease attention should be directed now to one aspect, now to another. In the case of kwashiorkor, the focal point of interest at the moment is the pancreas [see this *Bulletin*, 1948, v. 45, 635]. In discussing their observations on the salivary glands the Johannesburg workers have emphasized their *general* significance, as examples of the reactions of glandular tissue to malnutrition, and as clues to the nature of the relationship between parenchyma and interstitial tissue. But they also have an obvious *special* significance, because of the close morphological and functional similarity between salivary glands and pancreas.

The findings of Magahães Carvalho and his colleagues support the thesis that pancreatic damage is an important feature of kwashiorkor. The interpretation of the Brazilian results taken by themselves, would be difficult, since they were obtained during convalescence, and control subjects were not studied. However, they are in agreement with the work of VÉGHELYI in Budapest, who found a decreased secretion of pancreatic enzymes in babies not getting milk. This preceded the development of oedema and enlargement of the liver. These observations have not yet been published in detail.

There has been little experimental work on the reaction of the pancreas to dietary deficiencies. FRIEDMANN and FRIEDMANN produced atrophic changes in the acinar cells of the pancreas, together with fatty liver, in rats given a low protein, high fat diet. KRISTAL (*S. African J. Med. Sci.*, 1947, v. 12, 47) studied the pancreatic changes in rats fed on maize-meal porridge and fermented milk. These rats developed numerous lesions of the liver [see GILLMAN *et al.*, *Bulletin of Hygiene*, 1945, v. 20, 627]. Histological changes were found in the pancreas in 18 out of 30 rats. These changes included loss of granules, atrophy of acinar cells, cystic dilatation of ducts, fatty infiltration, and occasionally fibrosis.]

J. C. Waterlow

CHAUDHURI, R. N. & CHAKRAVARTI, H. **An Outbreak of Pellagra Syndrome in a Rural Area of Bengal.** *Indian Med. Gaz.* 1947, Nov., v. 82, No. 11, 657–60.

An outbreak of disease attributable to multiple deficiency of B-complex factors, in which a pellagroid dermatosis predominated, occurred in one section only of an Indian village. Exact dietary data are not reported, but it is evident that the diet of the whole village was deficient in protein and B vitamins. The only detectable difference between the diet of the affected families and that of those who showed no clinical manifestations was that the rice (which is the staple) of the affected group had many grains which were black in colour and bitter to the taste, whereas that of the affected families had none. The black rice all came from one small area, where the affected families had their paddy fields and where there was scarcity of water.

It was at first considered that the " black " degenerate grains might have lost most of their content of B vitamins ; but their nicotinic acid content proved, upon analysis, to be within normal limits. It is possible that these " black " grains contained a toxic substance which precipitated the occurrence of the deficiency state.

Dean A. Smith

BORROW, A., FOWDEN, L., STEDMAN, M. M., WATERLOW, J. C. & WEBB, R. A. **A Growth-retarding Factor in Maize Bran.** *Lancet.* 1948, May 15, 752–3, 1 fig.

An outstanding feature of endemic pellagra is its frequent association with the consumption of maize as a staple cereal. AYKROYD and SWAMINATHAN showed [this *Bulletin*, 1940, v. 37, 797 ; *Bull. Office Internat. d'Hyg. Publique*, 1941, v. 33, 507] that this cannot be explained on the basis of nicotinic acid deficiency alone. In the search for a toxic or pellagragenic factor in maize it has been shown that this cereal, if fed in sufficient quantities, exercises a growth-retarding influence in rats (WOOLLEY, *J. Biol. Chem.*, 1946, v. 163, 773 ; KREHL, HENDERSON, DE LA MUERGA and ELVEHJEM, *ibid.*, v. 166, 531), the latter workers attributing the effect to amino-acid imbalance, especially in respect of tryptophane.

In 1947, two of the present authors investigated an apparent increase in pellagra in Basutoland and found evidence that this increase was related to an increase in the consumption of maize bran resulting from changes in milling practice.

Feeding tests have now been made upon weanling mice by means of firstly, a diet containing 10 per cent. bran, secondly, a diet comprising mostly bran-free maize flour and a standard diet. The diets contained 10 per cent. protein and were designed to avoid, as far as possible, any amino-acid imbalance, tryptophane being available in equal amounts in the test and control diets.

The animals fed upon the 10 per cent. bran diet showed a highly significant growth retardation when compared with control litter-mates. No such growth-retardation occurred in the animals fed upon the maize flour diet, nor in a series fed upon the 10 per cent. bran diet to which 5 mgm. nicotinamide per 100 gm. had been added.

This evidence most strongly suggests that the toxic factor in maize, whose effect for rats and mice is growth retarding, resides in the bran fraction, and that the bran-effect is preventable by nicotinic acid. Extraction of the toxin has not yet been achieved.

As the authors emphasize, retardation of growth in mice has no necessary reference to human pellagra. It is, however, of the greatest importance to determine whether the factor in maize bran which has been shown to be growth-retarding for mice is toxic to man and whether it has any relation to pellagra. The results of work on these lines, which is now going on, may prove an important step in elucidating the aetiology of endemic pellagra.

Dean A. Smith

FRANKLAND, A. W. **Deficiency Scrotal Dermatitis in P.O.W.s in the Far East.** *Brit. Med. J.* 1948, May 29, 1023–6. [19 refs.]

Scrotal dermatitis associated with dietary deficiency was extremely prevalent among allied prisoners of war in the Far East. The present description is based upon 551 cases observed on Singapore Island.

Four forms, or degrees, of the condition were recognizable clinically. (i) Mild acute dry, in which there was redness and irritation of the scrotum; under treatment, or sometimes spontaneously, a fine desquamination left apparently normal skin. (ii) Severe chronic dry, bright red erythema extending to thighs, penis, perineum and anal region. (iii) Chronic wet, weeping dermatitis of scrotum and thighs, which without treatment often developed into (iv) ulcerated and oedematous, with great swelling, heavy secondary infection, sometimes with *C. diphtheriae*, progressing in the worst cases to spreading gangrene which, with marked generalized toxic symptoms, sometimes terminated fatally.

The incidence of the condition was highest when the riboflavin content of the diet was low: conversely when the latter could be kept at an adequate level cases did not occur. Associated deficiency diseases, both in individuals and in general incidence, were those usually attributed to hypo-riboflavinosis, namely glossitis, cheilosis, angular stomatitis, and corneal degeneration.

Some success was achieved by various forms of local treatment, but this was often incomplete and the relapse rate high. On the other hand, Marmite appeared to have a specific curative effect in uncomplicated cases and greatly hastened recovery in those cases for whose secondary infection local treatment was necessary.

The aetiology of the condition is discussed and it is concluded, on a considerable weight of evidence, that this form of scrotal dermatitis is due to deficiency of riboflavin or of some factor closely allied to it. *Dean A. Smith*

Chen Tzu-Ta. **Angular Blepharitis in Ariboflavinosis—a not well known Clinical Manifestation of Riboflavin Deficiency.** *Chinese Med. J.* 1948, Jan., v. 66, No. 1, 1–4.

"Three cases of angular blepharitis occurring as a manifestation of ariboflavinosis are described. A survey in a prison in Nanking was made. Twenty-three out of the 97 prisoners examined were found to have ariboflavinosis and 4 out of these 23 had angular blepharitis. This sign has not yet received much attention as a clinical manifestation of ariboflavinosis."

DERMATOLOGY AND FUNGUS DISEASES

Salvin, S. B. **Complement Fixation Studies in Experimental Histoplasmosis.** *Proc. Soc. Exper. Biol. & Med.* 1947, Nov., v. 66, No. 2, 342–5, 2 figs. [11 refs.]

In some recent work on the complement-fixation test for the diagnosis of histoplasmosis, by Tenenberg, Howell, Furcolow & Bunnell [this *Bulletin*, 1948, v. 45, 644], and by Cross & Howell [this *Bulletin*, 1948, v. 45, 643] the antigens used were histoplasmin (a filtered autolysate of the mycelial growth of *Histoplasma capsulatum*) and the polysaccharide extracted from histoplasmin. Salvin, on the other hand, used, as antigen, the intact, formalin-fixed, yeast-like form of the fungus, designated "YP", which was cultivated on a special medium devised by him [*Bulletin of Hygiene*, 1948, v. 23, 360].

Rabbits inoculated intravenously with living cultures of *Histoplasma capsulatum* in the yeast form, yielded an antiserum which reached its highest titre (about 1 : 512) in 30 days. Six different strains of *H. capsulatum* were used and the sera of 15 immunized animals were tested for complement-fixation with the YP and crude histoplasmin antigens. All of the sera reacted strongly with the YP antigen, the highest titre being 1 : 512; but only 8 reacted with the histoplasmin antigen, the highest titre not exceeding 1 : 128.

On the matter of the specificity of the complement-fixation test for histoplasmosis, the YP antigen gave no reaction whatever with 10 human sera from cases of coccidioidomycosis, 8 anti-*Coccidioides* rabbit sera, 8 anti-*Blastomyces* rabbit sera and 4 anti-*Candida* rabbit sera, but the histoplasmin antigen gave a reaction, albeit in low titre, with some of the sera in each of these groups. The specificity of the complement-fixation reaction with the YP antigen was also demonstrated in a test with 30 human sera from healthy persons and 2 sera from cases of histoplasmosis. *J. T. Duncan*

HEAT STROKE AND ALLIED CONDITIONS

Nelson, N., Eichna, L. W., Horvath, S. M., Shelley, W. B. & Hatch, T. F. **Thermal Exchanges of Man at High Temperatures.** *Amer. J. Physiol.* 1947, Dec. 1, v. 151, No. 2, 626–52, 15 figs.

In the study of physiological responses to high environmental temperatures, there is a great need for relationships to be established whereby the thermal stress imposed by the environment can be described in terms of the various factors which together make up that environment. The present paper describes a calorimetric study of the thermal exchanges between man and his environment. The total heat exchange was broken down into its several components, and physical constants were determined. The observations were made on

healthy young men exposed to dry bulb temperatures ranging from 90° to 120°F. with wet bulb temperatures of 70° to 91° and wind speeds of 30 to 600 feet per minute. Experiments were done with the subjects standing nude or clothed, and walking while clothed. The walking tests were done on a treadmill at a speed of three miles per hour with a three per cent. gradient. The metabolic rates while walking were about 160 Cal. per sq. m. per hour. The temperature and humidity of the air, the speed of air movement, and the radiation from the walls were measured during each test period. Measurements on the subjects included rectal temperatures, skin temperatures at various points, surface temperatures of clothing, oxygen consumption, heart rate, evaporated sweat loss and total sweat loss. From the temperatures of the skin and of the surface of clothing, weighted mean skin and surface temperatures were calculated.

In nude subjects, the maximum coefficient of evaporation varied as the 0·4 power of the air velocity. It is remarked that in evaluating the influence of wind speed and vapour pressure on the rate of evaporation the study must be confined to conditions where the skin or clothing surface is completely wet. With low rates of sweating, the rate of evaporation is not influenced by wind speed. Sweating rates high enough to measure the maximum coefficients of surface evaporation in clothed men were probably not reached, but charts are given which show the coefficients actually found.

The coefficients of convection vary as the square root of the air velocity. The convection coefficients for clothed subjects were 23 to 24 per cent. higher than those for nude subjects. This is in agreement with the estimated differences between the surface areas of clothed and nude men.

The radiation coefficients of nude subjects agreed with the theoretical value based on emissivities of wall and skin of 1, and a radiation area of 91 per cent. of the geometric area of the body. For some unaccountable reason, the coefficients of radiation for clothed subjects were much lower than would be predicted from reasonable assumptions as to the surface area and emissivity of the clothing.

Movement of the arms and legs while walking resulted in an increase in the apparent wind speed. When the men were walking at three miles per hour, this apparent increase was 150 feet per minute above the wind speed in the tunnel.

T. Bedford

Nelson, N. A., Shelley, W. B., Horvath, S. M., Eichna, L. W. & Hatch, T. F. **The Influence of Clothing, Work, and Air Movement on the Thermal Exchanges of Acclimatized Men in various Hot Environments.** *J. Clin. Investigation.* 1948, Mar., v. 27, No. 2, 209–16, 4 figs.

Partitional-calorimetric studies were made of four well-acclimatized young male subjects. They were acclimatized by walking for four hours a day, while dressed in twill uniforms, in an environment with a dry-bulb temperature of 120°F. and a wet bulb of 88°F. The calorimetric tests were carried out in a wind tunnel placed inside the laboratory hot room. The men stood or walked on a treadmill. The walking was at a speed of 3 miles per hour with a grade of three per cent. Walking caused an average energy expenditure of 160 Cal. per sq. m. per hour and standing caused one of 55 Cal. per sq. m. per hour. Seven temperature levels were studied. In these the dry bulb temperature ranged from 90° to 120°F. and the wet bulb from 70° to 88°F. At each temperature level, wind velocities of 30, 75, 150, 300 and 600 ft. per minute were employed. At each condition, three men were studied standing nude, standing clothed and walking clothed. The men spent 7½ hours in the heat each day except Sunday.

Increasing the wind speed from 30 to 600 feet per minute did not produce a striking change in the rectal temperature—in no case was the average rectal

temperature changed 1°F. Such an increase in air movement generally caused significant reductions in the skin temperatures of the subjects. The surface temperatures of clothed men followed the same pattern as skin temperature until the air temperature exceeded 96°F. With air temperatures higher than body temperature, the surface temperature of the clothed body rose with increasing air movement and occasionally reached 105°F. When the air temperature was 120°, the total sweat loss of clothed subjects was strikingly reduced by increase in air movement. With wet bulb temperatures of 88° or 91°F., increase in air velocity caused appreciable reductions in pulse rates.

The body heat production for a given amount of work remained unchanged irrespective of change in environmental conditions. When at high temperatures resting men wore clothing they gained less heat by convection and radiation than when they were nude, and therefore their evaporative heat losses were smaller. *T. Bedford*

Adolph, E. F. **Tolerance to Heat and Dehydration in Several Species of Mammals.** *Amer. J. Physiol.* 1947, Dec. 1, v. 151, No. 2, 564–75, 11 figs. [27 refs.]

Comparisons of tolerance to heat and dehydration were made between several species of mammals. The species considered were dogs, cats, rabbits, guineapigs, rats, and mice. These vary greatly in their capacities of evaporation, cooling, and in the tissue temperatures that they can endure. Together with body size, these appear to be the principal factors which determine tolerance to heat. A consistent sign of lethal conditions was found to be a rectal temperature of between 41·7° and 43·4°C. the critical value varying with the species. It appeared that heat stroke resulted from hyperthermic injury to regulatory tissues which were not identified. In some instances when animals had been subjected to gradual increase of rectal temperature and then cooled, death was delayed for periods up to 26 hours.

Dehydration through panting was copious in cats and dogs, but was limited in the other species. A considerable degree of dehydration did not bring about any change in the rate of evaporation loss. Dehydration rendered the animal very sensitive to warm atmospheres, presumably owing to the limitation of the circulation brought about by a depleted plasma volume. Failure of the circulation to transport heat to the surface caused an explosive rise of rectal temperature. In hot atmospheres animals that were allowed water to drink at will did not drink enough to maintain their body weights, and, except in the case of dogs with only small water deficits, when deprived of water they subsequently drank less than enough to recover their body weights. *T. Bedford*

Grocott, J. F. L. **Comfort Cooling in the Tropics.** *J. Inst. Heating & Ventilating Engineers.* 1948, Apr., v. 16, No. 153, 36–64, 9 figs. [28 refs.] Discussion 64–79.

In planning an installation for cooling buildings in the tropics one should be able to ascertain the following meteorological data :—

(*a*) maximum temperature for each month and season ;
(*b*) average maximum for each month ;
(*c*) average summer maximum ;
(*d*) the number of days on which the average summer maximum is exceeded in steps of 3°F., *e.g.*, if average maximum is 110°F. how often is 112° exceeded and how often 115° and so on.

Design recommendations are made on the basis of the experience of the Anglo-Iranian Oil Company during the past 20 years. When the external

temperature ranges from 90°F. to 125°F. the internal temperature should be 75° to 83°. This range has been used as the basis for all buildings except the general hospital. In the hospital, a uniform condition of 75°F. with 50 per cent. relative humidity is required in summer, while in winter the requirement is 70°F. with 30 to 50 per cent. relative humidity. In operating theatres a temperature of 70°F. with 50 per cent. relative humidity is demanded all the year round, although the external temperature ranges from 40°F. to 120°F. The changes between external and internal conditions are sometimes very great. Experience has revealed no ill-effects of these contrasts, while great benefits have accrued to the patients.

There are notes on the relation of building construction to air cooling. Modern buildings are constructed on the conventional lines of similar buildings in temperate zones. The roofs are mostly flat, or of slight pitch, and constructed of tile on insulation. Full advantage is taken of verandas, canopies, Venetian slats, etc., to exclude sunlight, and most buildings are finished in light colour. There is also a detailed discussion of the appropriate methods of cooling various types of buildings. *T. Bedford*

MISCELLANEOUS DISEASES

Fain, A. Contribution à la pathologie du Congolais. [**Notes on Pathological Conditions among the People of the Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Dec. 31, v. 27, No. 4, 433–40.

Limbos, P. Quelques notes au sujet de la pathologie indigène dans l'Uélé. [**Notes on Pathological Conditions in Uélé.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Dec. 31, v. 27, No. 4, 441–4.

Drummel, G. Note schématique sur la pathologie des indigènes au Kwango. Observations de 1938 à 1945. [**Descriptive Note on Pathological Conditions among the Africans in Kwango between 1938 and 1945.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Dec. 31, v. 27, No. 4, 429–32.

Bettolo, A. & Lugo, G. Contributo isto-patologico allo studio della gangosa (rino-oro-faringite mutilante dei tropici). [**Histological Study of a Case of Gangosa.**] *Acta Med. Italica.* 1948, Feb., v. 3, No. 2, 32–8, 10 figs. [13 refs.] English summary.

The authors relate the case of an Arab woman, 52 years of age, who had first shown signs about 20 years ago, of a small painless nodule affecting the left nostril, rapidly breaking down and spreading till much of the nose, mouth and face was destroyed by a typical gangosa. A series of photographs depicts graphically the terrible state of this unfortunate woman. Search for *Myco. leprae* and for *Myco. tuberculosis* was repeatedly negative; also for *Treponema pertenue*, leishmania, rhinoscleroma and blastomycetes. The W.R. had once been reported positive, in 1939, but was negative in each of the next three years; the Kahn and Meinicke tests were always negative. All sorts of treatment were tried: arsenicals, mercury, bismuth, antimonials, sulphonamides, X-rays, etc., but all in vain and the patient died.

Histological examination of the various tissues and organs was made: of different parts of the local lesions, of the lungs, heart, liver, spleen and kidneys. Photomicrographs indicate the conditions found, but there is nothing characteristic in them and none of the changes characteristic of leprosy, tuberculosis (including lupus), syphilis, or rhinoscleroma was to be made out and the authors see no reason for regarding gangosa as a complication or sequela of

yaws; they incline to the view that it is distinct from all of these, in short, that it is a condition *sui generis*, or in the medical jargon of to-day a "separate clinical entity." *H. Harold Scott*

ORTNER, E. Ueber Lathyrismus. [**On Lathyrism.**] *Wien. klin. Woch.* 1948, May 7, v. 60, No. 18, 291–3. [11 refs.]

The author states that in the concentration camp at Vapniarka, near Odessa, lathyrism was very rife. Of about 1,400 inmates, 800 or 57 per cent. showed the disease in an early or late stage. In September 1942, 1,200 men came to the camp; they had been in confinement for more than two years in different Rumanian prisons on "political or racial grounds." They were in a poorly nourished state and their food in the camp consisted of only 400 gm. of cooked *Lathyrus sativus* and 200 gm. of bread made of 80 per cent. barley meal and 20 per cent. chopped straw. Their chief complaints were of cramps, mostly in the calves, but also in the arm muscles; strangury and frequency of micturition, up to 20 times a day. Within two months walking became increasingly difficult, with spastic paresis. Ulcers would form on the toes, especially the big toe, and progress to gangrene, in many cases symmetrical and ending fatally. Three cases are described in detail. *H. Harold Scott*

ENTOMOLOGY AND INSECTICIDES: GENERAL

ANDUZE, P. J. Fauna hematófaga del Distrito Maturín (Est. Monagas, Venezuela): los Culicidos. [**The Mosquitoes of Maturin District, Monagas, Venezuela.**] *Rev. Med. Vet. y Parasit.* Caracas. 1947, Jan.–Dec., v. 6, Nos. 1/4, 121–6.

STAGE, H. H. **DDT to control Insects affecting Man and Animals in a Tropical Village.** *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 759–62, 1 fig.

During a period of five weeks in March and April 1946, all animals (except three calves) and all surfaces of buildings, inside and out, in Moengo, a village in Surinam, South America, were treated with either 2·5 per cent. DDT suspension in water or with 5 per cent. DDT oil solution.

The author describes the formulations, spraying equipment and the methods of trapping and then notes the effectiveness against certain insects. After two weeks, mosquitoes were difficult to find in cowbarns, but they began to be caught again after ten weeks. The numbers in light traps in the centre of the village fell from 900 and 400 to 13 and 3 respectively, a few days after treatment, "later there were even fewer". At breeding places where there were no buildings or animals within half a mile, the number of mosquitoes increased by 200 to 300 per cent. after ten weeks. In a house treated with the DDT suspension, mosquitoes were released two to three months after treatment and all were dead in three to four hours; after eleven months, 2,000 others were released and all were dead in eight hours; after fifteen months, 2,000 were released and 60 per cent. were dead after seven hours. In a similar house treated with the DDT oil solution, 2,000 mosquitoes were released after eleven months, some were still alive after 24 hours, but 50 hours later only two could be found alive. The species used in these tests are not named, but a complete analysis is to be published elsewhere. A list of species found in the locality is given.

Horn flies, bed-bugs, fowl ticks (*Argas persicus*), and chigoes (*Tunga penetrans*) are thought to have been eradicated. The number of cockroaches (? *Periplaneta americana*) is said to have been reduced by 90 per cent. and there was a

reduction in the number of cattle ticks (*Boophilus annulatus microplus*). The programme for dealing with dog fleas broke down, and dogs are still infested.

H. S. Leeson

LABORATORY PROCEDURES

BLACK, R. H. **Leishman's Stain adapted for Use with Histological Sections.** *Ann. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1, 52–3, 3 figs. on 1 pl.

This method is recommended as an alternative to Giemsa's stain for sections, particularly to demonstrate the erythrocytic and exoerythrocytic forms of *Plasmodium gallinaceum*. Thin sections are treated for 5–10 minutes with a saturated aqueous solution of picric acid. They are then washed in water and stained for 25 minutes with a mixture consisting of one part of Leishman's stain with two parts of distilled water. This should be freshly prepared. The section is then immersed in running water for about 10–15 minutes, dehydrated in xylol-acetone mixtures and mounted in a neutral mounting medium. Van Gieson's strain was originally employed, but tests showed that it was the picric acid constituent which was responsible for the good results. This substance appears to act by virtue of its acidity ; its *p*H was 12, and when decinormal hydrochloric acid was substituted for picric, essentially similar results were obtained. The tissue cells stain brilliantly and in some organs, differentially. In the kidney, for instance, the collecting tubules are stained magenta, while other tubules give a different reaction. Malaria parasites in red blood cells are easily recognized, and exo-erythrocytic forms are very deeply stained.

The author admits that the method is not an improvement on Giemsa's stain and the absence of differential staining of the chromatin and the cytoplasm of parasites will detract from its value in protozoology. *P. C. C. Garnham*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

NEDERL. TIJDSCHR. V. GENEESK. 1948, May 22, v. 92 (ii), No. 21, 1566–80, 2 graphs. Nederlandsche vereeniging voor tropische geneeskunde. Vergadering op zondag 28 September 1947 te Utrecht [HULSHOFF, A. A., President]. [**Netherlands Association for Tropical Medicine.**]

Four subjects were dealt with at this meeting, held at Utrecht in September, 1947 : plague, tetanus, the beriberi heart and malaria.

Two methods of campaign against plague have prevailed in Java : re-housing of the indigenous population, with protection against rat intrusion and prophylaxis by means of living plague vaccine. The vaccination languished under Japanese occupation and the occurrence of abscesses after inoculation raised the suspicion that these were mitigated plague lesions. These were, however, only manifestations of contamination by pyogenic organisms and the plague bacillus in question was proved to be still quite avirulent. In the restoration of the vaccine of Otten the Harbin strain has now been left out and only the original Tjiwidej strain used. The latter strain immunized the guineapig in minimal doses, but not the house rat. It is the guineapig which comes closest to man in its " immunological response " and the Tjiwidej strain is therefore to be preferred for routine use. Protection is reckoned to last for three months unaltered and to a less degree for an entire year.

A close argument on the characteristics of the beriberi electrocardiogram was presented by AALSMEER mainly to show how this differed in oriental regions from that of America and the west. The conclusion seems to be reached that the western beriberi heart is not of the same type as the oriental *shoshin* and that recognition of an alcohol-beriberi heart must be given consideration.

Malaria is treated under the heading of "Colonization Kesilir," which signified really the establishment by the Japanese of a concentration camp in a region full of all the possibilities of intense malaria infection. The vector mosquito was *A. aconitus*. Very careful work was done both in the way of records and of quinine prophylaxis. The records, which would have given valuable information on the incidence of relapses and fresh infections, were lost. A most fortunate circumstance in this camp was that quinine was available in abundance which, with the energetic measures adopted to deal with the mosquito menace, served to bring malaria under medical control. This régime followed on the first explosive outbreak of malaria. Orderlies were appointed who made daily visits to their sector of the camp. Slight cases of sickness were reported and examined the same day. If the patient had fever, a thick drop preparation was made of his blood and if it was positive he received a first treatment of 30 tablets of bisulphate of quinine—6 each day, of 220 mgm. each. After a week's interval he received the same 5-day course again. A table showing the frequency distribution of attacks in 295 cases is given, where the greatest number, 130, suffered only one attack and the numbers fell steadily to 3 cases with 9 attacks each. *W. F. Harvey*

POPPER, L. Medizinisches aus Bolivien. [**Medical Notes from Bolivia.**] *Wien. Klin. Woch.* 1948, May 14, v. 60, No. 19, 297–301.

An interesting though short account of the diseases met with in Bolivia prefaced by some facts on the physical geography of the country. There are [or were, at the time of writing] 500 doctors practising there, most of them in the towns. *Tuberculosis* has been recorded as common among the soldiers, and the author's predecessors have stated that 7 per cent. of the regiment of 400 die of it. The author, therefore, undertook an investigation, examining all recruits. An intracutaneous test showed 38 per cent. reacting positively. Further observation of the members of one unit discovered no cases in the next three months. Later, some, especially those who had not reacted to tuberculin, developed an exudative pleurisy and a few of them actual pulmonary tuberculosis. By careful attention the fatality rate fell from 7 to 1 per cent. Another unit, not so controlled and watched over, and housed in unfavourable conditions, had a 10 per cent. mortality in six months. Symptoms, in the earlier stages at least, are very slight. In the following year 3,540 men were kept under observation and among them were 65 cases of pulmonary tuberculosis, 58 of exudative pleurisy, and 19 of other forms, 142 in all, or 4·0 per cent. morbidity [not 152 and 4·3, as stated.] *Dysentery* also is fairly rife, some amoebic but more commonly bacillary—the water, from ponds and wells, is often contaminated. *Leishmaniasis* is not seen in Chaco, but occurs in north-east Bolivia. Other ulcerous conditions met with are phagedaena (associated with spirochaetes and fusiform bacilli and occasionally diphtheroids) and blastomycosis, but this last is uncommon. The author has seen one case of coccidioidomycosis. *Malaria* is, of course, present, mostly benign tertian, the relative frequencies of benign tertian, subtertian and quartan are said to be 30 : 3 : 1. Chronic malaria is often afebrile, but the parasite can nearly always be found ; it was missed in only 4 per cent. of 600 cases. No case of blackwater fever was seen by the author. Nutrition is poor and consequently resistance to disease is low. The average diet for an adult is only 1,600–1,800 calories

and that mainly made up of carbohydrate. In the Bolivian highlands, the amounts consumed per head per year are 21 kgm. meat, 36 litres of milk and 0·22 kgm. of fat—" the lowest in the world." In the lower levels where cattle are reared, the quantities of meat and milk are greater, but the calorie value is lower. The soldier's ration is about 3,000 calories, but the constituents are badly balanced.

Hookworm infestation is widespread and severe anaemia is far from uncommon; both *Ancylostoma* and *Necator* are the cause. About 30 per cent. of recruits were passing hookworm ova, 20 per cent. *Ascaris*, 15 per cent. *Trichuris*, and 6 per cent. *Strongyloides stercoralis* ova. *Balantidium* also is common. *Filariasis*, especially *M. ozzardi*, is often met with. *Chagas's disease* is not very common in spite of the fact reported by many that *Triatoma infestans* and *Panstrongylus megistus* were seen, and the author found more than half of them infected. *Leprosy* was occasionally seen. *Yellow fever* has been almost stamped out by the efforts of the Rockefeller Foundation. Eaters of Coca suffer from pareses and neuro-muscular atrophy, especially of the peroneal area, and from hyperaesthesia and anaesthesia of the conjunctiva; later, those who indulge in this habit become wrecks and succumb readily to intercurrent disease. *Venereal diseases* are not rife; *lymphogranuloma inguinale* is fairly common. Of the infective fevers, *diphtheria* is rare, *scarlet fever* practically unknown, *measles* occurs inland and among adults; *whooping-cough* in children is usually mild. *H. Harold Scott*

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Snow, J. S., Satulsky, E. M. & Kean, B. H., 695.
Soman, D. W., 701.
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de Souza Lima, L., 714.
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Tanamal, S. J. W., 706.
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Walker, H. A. & Richardson, A. P., 688.
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Wallace, F. G., Mooney, R. D. & Sanders, A., 722.
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——, Hardman, N. F., Burgess, R. W., Frohne, W. C. & Sabrosky, C. W., 674.
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